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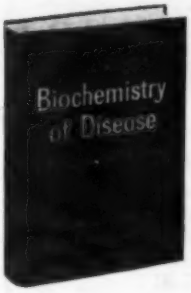
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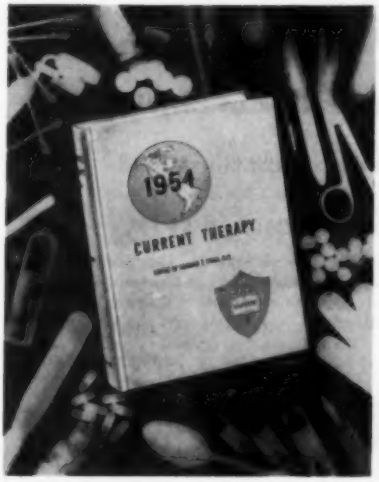
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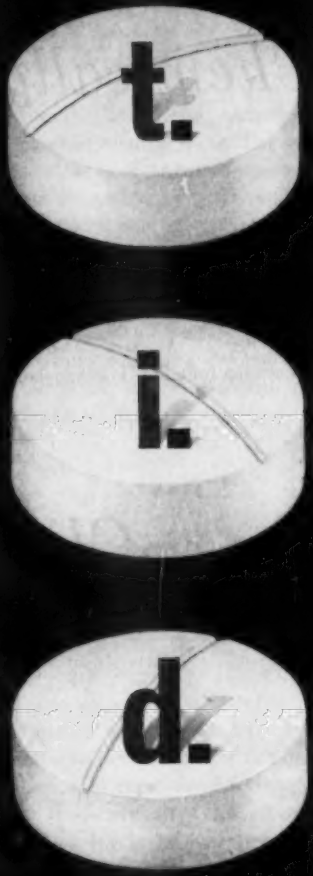
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METAMINE, newest of the long-acting coronary vasodilators, has the smallest effective dose: 2 mg. Taken routinely, METAMINE prevents attacks of angina pectoris or greatly diminishes their number and severity. Even during prolonged or excessive dosage, side effects are mild and infrequent. Tolerance and methemoglobinemia have not been reported.

The beneficial actions of METAMINE appear to affect the entire circulation, not just the coronary and myocardial vessels, reducing the work load and oxygen requirement of the heart and permitting a life of useful activity for the anginal patient who might otherwise become another cardiac cripple.

for prevention of angina pectoris



Numerous clinical and experimental studies since 1946 indicate that METAMINE is ideally suited for routine prevention of anginal attacks because of low (2 mg.) effective dose, prolonged action, and exceptional freedom from side effects and tolerance. Blood pressure is not altered. Finally, while slower to act than nitroglycerin, METAMINE "exerts a more prolonged and as good, if not slightly better, coronary vasodilator action . . ." (Melville, K.I., and Lu, F.C.: *Canadian M.A.J.*, 65:11, 1951.)

DOSAGE: To prevent angina pectoris, swallow 1 METAMINE tablet after each meal, and 1 or 2 tablets at bedtime. Full preventive effect is usually attained after 3rd day of treatment.

Thos. Leeming & Co. Inc.

155 EAST 44TH STREET, NEW YORK 17, N.Y.

Anemia in the Presence

Many anemic patients continue to show a subnormal blood picture despite adequate iron therapy. Furthermore, ample systemic iron reserves have been demonstrated in many markedly anemic patients. In such cases, depression of the hemopoietic function due to bacterial or virus infection, or to allergy, is very frequently the cause of the anemia.

This accounts for the poor response so often reported where iron alone has been given[1], in "low-grade anemias" of children[2], nutritional anemia[3] and other forms of "secondary" anemia.

Such limited response has raised the question—is iron the complete answer to basic anemia therapy?

Recent research[4,5] suggests that the answer is NO—a more *basic* approach should aim at stimulating the depressed bone marrow, the "organ" responsible for effecting erythrogenesis, mobilization of iron reserves and hemoglobin synthesis.

RONCOVITE*

The First True Hemopoietic Stimulant

Roncovite offers, for the first time, the specific bone marrow hemopoietic action of well-tolerated cobalt plus adequate supplementary iron for those lacking in "systemic iron reserves."

In iron deficiency anemia—

where iron has been the standard treatment—Roncovite produces a faster response, greatly superior erythropoiesis and up to fourfold increases in the utilization of iron.[4]

In anemia accompanying infection

or chronic inflammatory disease—*where iron is useless*—Roncovite induces, in many cases, a striking and dramatic hemopoietic response.[6]

Rapid Improvement—

The patient often voluntarily reports an increased sense of well-being *within a few days*—as reported by documented clinical evidence.

SAFE—

Even During Sustained Use

Cobalt has the same low order of toxicity as iron. Moreover, cobalt is rapidly and almost completely excreted via the urine, so that there is little if any cumulative effect even after periods exceeding 100 days of continuous parenteral use. The body shows no significant amounts of cobalt 48 hours after the last dose.

*The Original, Proved Cobalt Product.

of Iron?

NEW EVIDENCE: Effect of Roncovite Drops (Cobalt-Iron Therapy) in Selected Cases of Iron Deficiency in Infants and Children.[4]

Age in Mos.	Complicating Illness	R. B. C. Increase per day	Hgb. Increase per day
1	Neonatal Jaundice	40,000	0.08 Gm.
3	None	113,000	0.22 Gm.
17	None	74,000	0.15 Gm.
5	Acute Laryngo-Tracheitis	—500	—0.01 Gm.
10	None	79,000	0.22 Gm.
15	None	133,000	0.20 Gm.
3½	Infantile Diarrhea	19,000	0.03 Gm.
11	None	26,000	0.07 Gm.
17	Herpetic Stomatitis	100,000	0.11 Gm.
9	None	159,000	0.11 Gm.
14	None	155,000	0.14 Gm.
12	Cervical Lymphadenopathy	165,000	0.12 Gm.
15	None	68,000	0.10 Gm.
13	None	190,000	0.28 Gm.
6	Gastro-enteritis	198,000	0.16 Gm.
9	None	42,000	0.09 Gm.
24	None	81,000	0.16 Gm.
19	Fever	78,000	0.15 Gm.
7	Urinary Infection	134,000	0.10 Gm.
24	None	122,000	0.15 Gm.
16	Staph.-Adenitis	77,000	0.07 Gm.
12	None	107,000	0.15 Gm.
15	None	134,000	0.10 Gm.

SUPPLIED:

Roncovite Tablets—enteric coated, red. Each contains cobalt chloride, 15 mg.; ex. ferrous sulfate, 0.2 Gm.; bottles of 100.
Dose: one tablet 4 times a day.

Roncovite Drops—each 0.6 cc. contains cobalt chloride, 40 mg.; ferrous sulfate, 75 mg.; bottles of 15 cc. with calibrated dropper.
Dose: 0.6 cc. daily.

REFERENCES:

1. Josephs, H.: J. Pediat. *49*:246 (1931).
2. Cass, L. J.; Frederick, W. S., and Di Gregario, S.: Journal-Lancet *51*:73 (1953).
3. Kato, K.: J. Pediat. *11*:385 (Sept.) 1937.
4. Rohn, R. J.; Bond, W. H., and Klotz, L. J.: J. Indiana St. Med. Assoc. *46*:1253 (Dec.) 1953.
5. Rohn, R. J., and Bond, W. H.: Journal-Lancet *73*:301 (1953).
6. Wolf, H.: Med. Monatrsshr. *5*:239, 1951.

LLOYD BROTHERS, Inc.
Cincinnati 3, Ohio

Aminodrox

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Heard at the staff meeting . . .



increases the usefulness of oral aminophylline

send for detailed literature and sample

THE S. E. MASSENGILL CO.

BRISTOL, TENNESSEE

In the form of AMINODROX, three out of four patients can be given therapeutically effective *oral* doses of aminophylline.

This is possible with AMINODROX because gastric disturbance is avoided.

How congestive heart failure, bronchial and cardiac asthma, status asthmaticus and paroxysmal dyspnea can be treated successfully with *oral* aminophylline in the form of AMINODROX.

Aminodrox Tablets contain 1 1/2 gr. aminophylline with 2 gr. activated aluminum hydroxide.

Aminodrox-Forte Tablets contain 3 gr. aminophylline with 4 gr. activated aluminum hydroxide.

Also available with 1/4 gr. phenobarbital.

A new, potent antibacterial—

Gantricillin-300 'Roche'

...for wide-spectrum antibacterial therapy: GANTRICILLIN®-300 'Roche.' Each tablet provides 300,000 units of penicillin PLUS 0.5 Gm of Gantrisin®, the single, highly soluble sulfonamide.

Combined antibacterial therapy —

...with the new Gantricillin®-300 tablet 'Roche.' A convenient way of administering 300,000 units of penicillin PLUS 0.5 Gm of Gantrisin®, the single, soluble sulfonamide.

The antacid as pleasant as an after-dinner mint

ALUDROX®

Aluminum Hydroxide Gel with Magnesium Hydroxide







For rapid relief of simple hyperacidity or the hyperacidity of peptic ulcer

When an antacid is prescribed, the physician wants medical effectiveness. When the antacid is taken, the patient wants palatability and convenience.

ALUDROX Tablets combine these qualities. They afford efficient antacid therapy. They are unobtrusive, pleasant to take . . . can be chewed and swallowed with or without water, wherever the patient may be. Tablets encased in handy cellophane strips, to fit pocket or purse.

Supplied:
ALUDROX Tablets,
boxes of 60

Also available:
ALUDROX Suspension,
bottles of 12 fl. oz.

ALUDROX

Wyeth
PHILADELPHIA 2, PA.

only Kolantyl gives him this four way



Compare the four way action of Kolantyl with your prescription for peptic ulcer.	Kolantyl	Your Rx
1 Antacid	✓	
2 Antipeptic	✓	
3 Antispasmodic*	✓	
4 Antilysozyme-Demulcent	✓	

*Bentyl — Merrell's distinctive antispasmodic that is more effective than atropine — free from "belladonna backfire".

The Wm. S. Merrell Company... *Pioneer in Medicine*

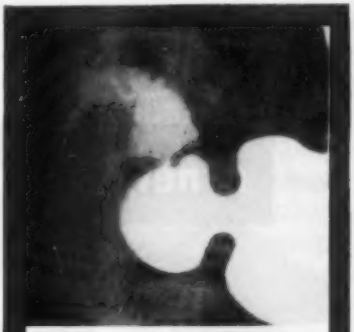
relief of peptic ulcer

controls *four* important etiologic factors

Every ulcer patient you see wants RELIEF—*prompt relief*. Only Kolantyl® provides these four therapeutic approaches to peptic ulcer: antacid, antipeptic, antispasmodic and antilysozyme-demulcent.

Your Kolantyl prescription represents one of the most complete peptic ulcer preparations available today. Give your next ulcer patient economical four way relief... prescribe good-tasting *Kolantyl*.

Kolantyl



Appearance of active duodenal ulcer after 12 weeks ambulatory treatment with diet and Kolantyl, marked clinical improvement.[1]

Prescribe Kolantyl for Prompt Relief of peptic ulcer, gastritis, hyperacidity.

action:

Antacid (magnesium oxide, aluminum hydroxide) for almost immediate, prolonged neutralization of acid without rebound.

Antipeptic (sodium lauryl sulfate) inhibits necrotic action of pepsin and lysozyme.

Antispasmodic (Bentyl) relieves painful spasm comfortably; superior to atropine.[2]

Demulcent (methylcellulose) provides a protective coating of the ulcerated area.

composition:

Each tablet or 10 cc. Kolantyl Gel contains:

Bentyl Hydrochloride	5 mg.
Aluminum Hydroxide Gel	400 mg.
Magnesium Oxide	200 mg.
Sodium Lauryl Sulfate	25 mg.
Methylcellulose	100 mg.

dosage:

Prescribe two to four teaspoonfuls Kolantyl Gel or two tablets (chewed for more rapid action) every 3 hours, or as needed for relief.

Gel supplied in 12 oz. bottles — Tablets in bottles of 100 and 1000.

1. MUFFORD, A. R.: MICH. STATE MED. SOC. 49:1308, 1950.
2. RICHARDS, G. AND BROWNE, D.: SOU. MED. J. 45:1139, 1952.

KOLANTYL® "BENTYL" T. M.

for 125 Years

New York
CINCINNATI
St. Thomas, Ontario

Merrell
Since 1828

PNEUMOCOCCI • MENINGOCOCCI • GRAM-NEGATIVE AND GRAM-POSITIVE COCCI • GRAM-NEGATIVE BACILLI • PNEUMOCOCCI • GRAM-NEGATIVE AND GRAM-POSITIVE COCCI • GRAM-NEGATIVE BACILLI • PNEUMOCOCCI • MENINGOCOCCI • GRAM-NEGATIVE AND GRAM-POSITIVE COCCI • GRAM-NEGATIVE BACILLI • PNEUMOCOCCI • GRAM-NEGATIVE AND GRAM-POSITIVE COCCI • GRAM-NEGATIVE BACILLI • PNEUMOCOCCI

a new broad-spectrum antibiotic

ACHRO

ACHROMYCIN is a new and superior broad-spectrum antibiotic, developed by Lederle research. ACHROMYCIN has demonstrated greater effectiveness in clinical trials with the advantages of more rapid absorption, quicker diffusion in tissue and body fluids, and increased stability resulting in prolonged high blood levels.

ACHROMYCIN has demonstrated effectiveness against pneumococcal and meningococcal infections; against Gram-negative cocci; against Gram-positive cocci; against Gram-negative bacilli; and against certain mixed infections.

CAPSULES { 250 mg. / 100 mg. / 50 mg. } TABLETS { 250 mg. } INTRAVENOUS { 500 mg. / 250 mg. / 100 mg. } SPERSOIDS® Dispersible Powder { 50 mg. per teaspoonful (3.0 Gm.)

Other dosage forms will become available as rapidly as research permits.

Please Mention this Journal when writing to Advertisers



broader tolerance
greater stability
faster absorption

Lederle

LEDERLE LABORATORIES DIVISION AMERICAN Cyanamid COMPANY 30 Rockefeller Plaza, New York 20, N.Y.

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Acute hypocalcemic tetany

(e.g., after total thyroidectomy) is swiftly controlled by Hytakerol together with calcium.



• dose

Orally 3 to 10 cc. (or 6 to 20 capsules) daily until tetany is relieved, weekly maintenance dose of 1 to 7 cc. or 2 to 14 capsules depending upon the blood and urine calcium levels. From 10 to 15 Gm. calcium lactate or gluconate should be given daily through the period of therapy.

• supply

Hytakerol in Oil, bottles of 15 cc.; Hytakerol Capsules (each equivalent to 0.5 cc.), bottles of 50.

Hytakerol®

Brand of dihydrotachysterol

Winthrop-Stearns INC.
NEW YORK 13, N. Y. WINDSOR, ONT.

Hytakerol, trademark reg. U.S. & Canada

reflects in your patients

a fresh response

and a

vigorous

improvement



armatinic *activated*

Vitamin B_{12} PLUS Intrinsic Factor

In Armatinic Activated, the hemopoietic factors activate and potentiate each other in their interrelated role in producing mature red blood cells.

Each ARMATINIC ACTIVATED Capsulette contains:

Ferrous Sulfate, Exsiccated	200 mg.
Vitamin B_{12} Crystalline	10 mcg.
Folic Acid	1 mg.
Vitamin C	50 mg.
Liver Fraction II (N.F.) with Desiccated Duodenum (contains Intrinsic Factor)	350 mg.

Supplied in bottles of 100 and 1000.

Also available: Armatinic Liquid, bottles of 8 oz. and 16 oz.

COMPREHENSIVE ANTIANEMIA THERAPY IN A SINGLE CAPSULETTE

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NOW

A safer tranquilizer-antihypertensive

Serpasil™

(RESERPINE CIBA)

A pure crystalline alkaloid of Rauwolfia serpentina

Serpasil, *a pure, crystalline, single alkaloid of* Rauwolfia serpentina, *produces* mild, gradual, sustained *lowering of blood pressure without undesired effects from unknown alkaloids of the whole root. Other advantages:*

- *Effective alone or in combination with other antihypertensive agents.*
- *Uniform potency.*
- *Predictable therapeutic results.*
- *No tolerance developed, or toxic effects reported; no contraindications; no serious side effects.*

Virtually every hypertensive patient may be treated with **Serpasil** *therapy. Prescribe this* safer *tranquilizer-antihypertensive now. Available at all prescription pharmacies.*

Serpasil *Tablets, 0.25 mg. and 0.1 mg., bottles of 100.*

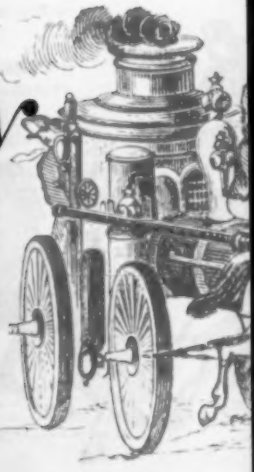
Ciba *Summit, New Jersey*

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new *concept*

in anti-inflammatory therapy

new *safety*



new

Potent in oral
systemic anti-inflammatory therapy

Cortril tablets

brand of hydrocortisone

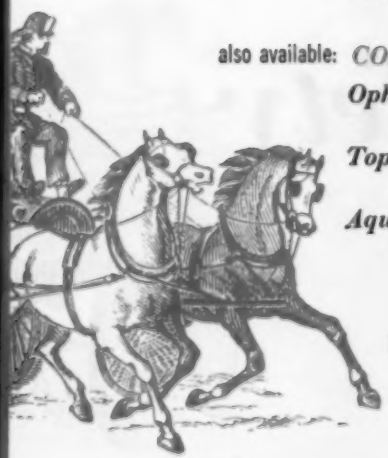
Studies indicate that hydrocortisone is the predominant natural anti-inflammatory hormone, and extensive investigations have demonstrated its superior therapeutic efficacy.

Clinical reports comparing hydrocortisone with cortisone note that hydrocortisone produces maximal therapeutic benefits with smaller initial and maintenance dosage requirements and decreased endocrine complications.[1,2]

Cortril
of proved therapeutic merit in:

- Rheumatoid arthritis
- Osteoarthritis
- Acute rheumatic fever
- Addison's disease
- Bronchial asthma
- Acute and chronic ocular disorders and other conditions responsive to systemic adrenocortical hormone therapy

supplied: CORTRIL Tablets, *scored, 10 mg. in bottles of 25*
20 mg. in bottles of 20



also available: *CORTRIL Acetate*

Ophthalmic Ointment
in 1/8-oz. tubes in strengths of 0.5% and 2.5%

Topical Ointment
in 1/6-oz. tubes in strengths of 1.0% and 2.5%

Aqueous Suspension for intra-articular injection
in 5-cc. vials, 25 mg. per cc.

PFIZER SYNTEX PRODUCTS

new

Anti-inflammatory and anti-infective management in ocular disorders

Cortril acetate ophthalmic suspension

brand of hydrocortisone acetate

with Terramycin® hydrochloride

brand of oxytetracycline hydrochloride

New therapeutic approach in ocular disorders

The combination in one preparation of CORTRIL, the topically effective anti-inflammatory hormone, and TERRAMYCIN, the broad-spectrum antimicrobial agent, represents a new attainment in ophthalmologic therapy.

Clinical studies reveal that topical hydrocortisone is significantly superior to cortisone[3,4,5] in reducing local edema and controlling excessive tissue reactions due to allergens, infection, or trauma in diseases of the anterior segment of the eye.

TERRAMYCIN, with its broad antimicrobial spectrum, is an antibiotic of choice to curtail the growth of primary or secondary infecting organisms. Thus in ocular inflammation where infection coexists, is suspected, or anticipated, administration of CORTRIL Ophthalmic Suspension with TERRAMYCIN provides unexcelled therapy.

Cortril with Terramycin

of distinct advantage in:

- **Blepharitis**
- **Conjunctivitis**
- **Corneal ulcer and other corneal afflictions**
- **Scleritis**
- **Iritis and other conditions responsive to topical adrenocortical hormone therapy**

supplied: Each cc. of CORTRIL Acetate Ophthalmic Suspension with TERRAMYCIN, sterile, contains 15 mg. of CORTRIL acetate and 5 mg. of TERRAMYCIN hydrochloride, in amber bottles of 5 cc. with a sterile eye dropper.

references:

1. Boland, E. W.: Ann. Rheum. Dis. 12:125, 1953. 2. Boland, E. W.: California Med. 77:1, 1952. 3. Laval, J.: A.M.A. Arch. Ophth. 59:299, 1953. 4. McDonald, F. R.; Leopold, I. H.; Vogel, A. W., and Mulberger, R. D.: A.M.A. Arch. Ophth. 49:400, 1953. 5. Steffensen, E. H.: J.A.M.A. 159:1660, 1952.

Pfizer

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Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, New York

providing a sound basis for vitamin dosage...



The "standard maintenance vitamin capsule" and the "therapeutic vitamin capsule" recently recommended in the National Research Council's publication, "Therapeutic Nutrition,"* bring new, authoritative dosage standards into the present complexity of multivitamin formulations and potencies.

Panalins, the standard maintenance vitamin capsule, is formulated in accordance with the recommendation* that such a supplement provide certain other vitamins in addition to the six for which Recommended Dietary Allowances have been established. One Panalins capsule daily assures vitamin protection for most patients.

Panalins-T is formulated in accordance with the recommendation* that acutely ill or injured patients receive a therapeutic capsule containing approximately five times the usual daily allowances of B complex vitamins and vitamin C.

Therapeutic Nutrition, Publication No. 234, National Research Council.



The need for two formulations

"The accepted standards of recommended dietary allowances apply to healthy individuals or to certain specific conditions such as pregnancy and lactation. Recent evidence has indicated that these normal allowances may not always be adequate for the sick and injured."*

Standard maintenance capsule for supplementation

"When supplementary vitamins are required, a standard vitamin capsule should be made available. This should contain several vitamins in addition to the six recommended by the National Research Council for normal healthy people."*

Therapeutic capsule for stress states

"A simple therapeutic capsule would contain approximately five times the usual daily allowances for the various vitamins."*

STANDARDS*

maintenance and therapy

PANALINS

N.R.C. STANDARD MAINTENANCE VITAMIN CAPSULE



Conforming precisely to the N.R.C. recommendation,† each Panalins Capsule supplies:

Thiamine	2 mg.
Riboflavin	2 mg.
Niacinamide	20 mg.
Ascorbic acid	50 mg.
Calcium pantothenate	5 mg.
Pyridoxine hydrochloride	0.5 mg.
Folic acid	0.25 mg.
Vitamin B_{12}	2 mcg.
Vitamin A	5000 units
Vitamin D	400 units

PANALINS-T

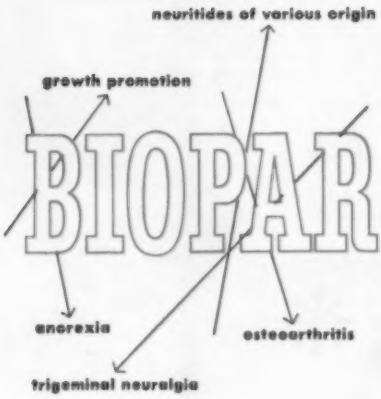
N.R.C. STANDARD THERAPEUTIC VITAMIN CAPSULE



Conforming precisely to the N.R.C. recommendation, each Panalins-T Capsule supplies:

Thiamine	10 mg.
Riboflavin	10 mg.
Niacinamide	100 mg.
Calcium pantothenate	20 mg.
Pyridoxine hydrochloride	2 mg.
Folic acid	1.5 mg.
Ascorbic acid	300 mg.
Vitamin B_{12}	4 mcg.

MEAD JOHNSON & COMPANY • EVANSVILLE, INDIANA, U.S.A. MEAD



with wide non-hematologic uses

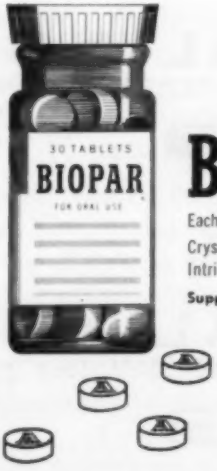
Biopar is exceedingly useful as an oral replacement for injectable vitamin B_{12} treatment, and as an adjunct to high-potency injections. A pronounced "tonic" effect is accredited to vitamin B_{12}.

BIOPAR is "intrinsically" better

A new, many times more potent Intrinsic Factor in Biopar makes possible a full therapeutic vitamin B_{12} response orally—even in the presence of partial or complete achlorhydria. The Intrinsic Factor in Biopar, many times more active than previously available intrinsic factor preparations—performs the essential functions ascribed to the classic Intrinsic Factor of Castle.

an effective oral replacement for injectable B_{12}

Oral Biopar therapy produces a full reticulocyte response and red blood cell increment in pernicious anemia, as confirmed by fourteen independent investigators (personal communications).



BIOPAR®

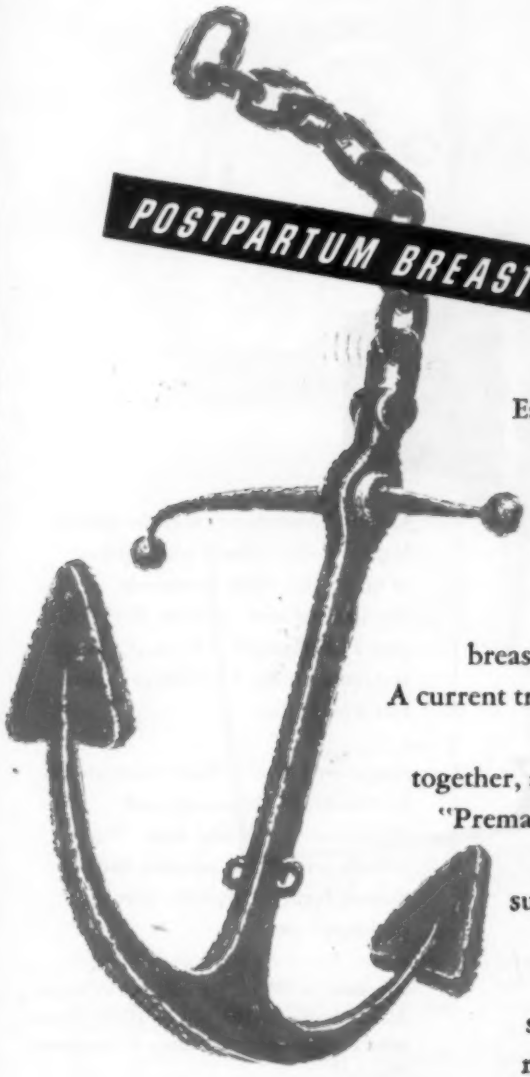
Each BIOPAR tablet contains:

Crystalline Vitamin B_{12} U.S.P.	6 mcg.
Intrinsic Factor	30 mg.

Supplied: Bottles of 30 tablets.

THE ARMOUR LABORATORIES

A DIVISION OF ARMOUR AND COMPANY · CHICAGO 11, ILLINOIS



POSTPARTUM BREAST ENGORGEMENT

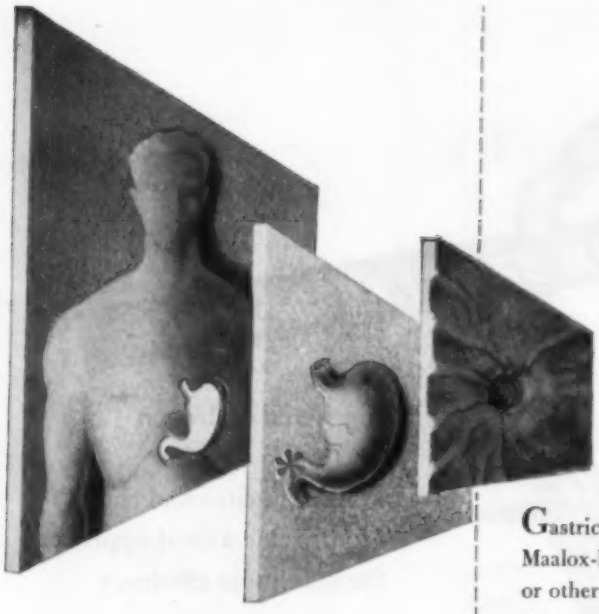
Estrogen and androgen
go together
like "anchor and chain"
to provide a dual approach
for maximum efficiency
in postpartum
breast engorgement.
A current trend of opinion is that
these two steroids,
together, as combined in
"Premarin" with Methyltestosterone,
will have a greater effect on
suppression of lactation
than either one alone.
Excellent results from
such therapy have been
reported by many clinicians.

"PREMARIN"® with METHYLTESTOSTERONE

for combined estrogen-androgen therapy

Ayerst, McKenna & Harrison Limited · New York, N.Y. · Montreal, Canada

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maalox®

gives ulcer relief

without side effects

Gastric hyperacidity is controlled by Maalox-Rorer without constipation or other side effects commonly encountered with antacids. Relief of pain and epigastric distress is prompt and long-lasting. Available in tablets and liquid form.

Suspension Maalox-Rorer contains the hydroxides of Magnesium and Aluminum in colloidal form. The smooth texture and pleasant flavor make it highly acceptable, even with prolonged use.

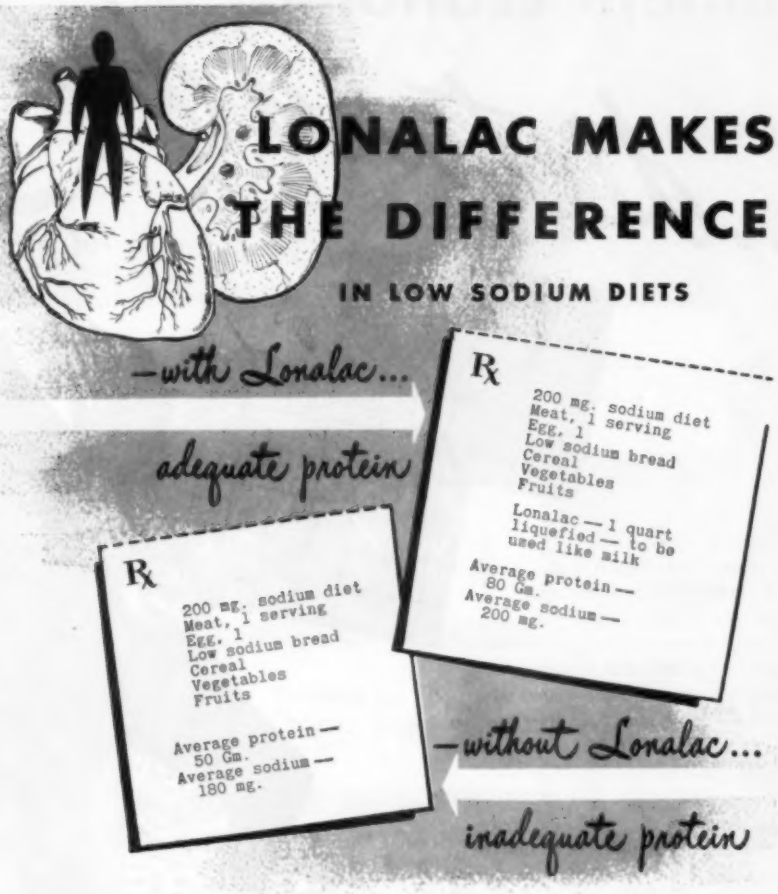
Supplied: in 355 cc. (12 fluid ounce) bottles. Also in bottles of 100 tablets. (Each Maalox tablet is equivalent to 1 fluidram of Suspension Maalox.)

Samples will be sent promptly on request.

WILLIAM H. RORER, INC.

Drexel Bldg., Independence Square

Philadelphia 6, Pa.



Nutritionally similar to whole milk but with negligible sodium content, Lonalac solves the problem created by the high sodium content of the usual protein foods.

When sodium intake must be sharply restricted, protein deficiency is seriously threatened . . . since meat and eggs can be used only in small quantities and milk, with its still higher sodium content, usually must be eliminated.

With Lonalac supplying the protein equivalent of milk, the patient's nutritional needs can be generously met, even on a 200 mg. sodium diet.

Lonalac is used just as milk is used, as a beverage and in soups, muffins, desserts, etc. It permits varied and appetizing meals that encourage patients to adhere to a low sodium regimen.

Lonalac is virtually free of cholesterol.

Lonalac is supplied in 1 pound and economical 4 pound cans. Low sodium diet outlines suitable for use by patients are available on request.

Lonalac

The low sodium, high protein food

MEAD JOHNSON & COMPANY • EVANSVILLE, INDIANA, U.S.A. MEAD

Eminent Economist ...dietary dub



He knows economy. Even economizes on his vitamin intake.

Eventually, he'll be studying a corrected diet and looking to you for a potent B-complex supplement like Sur-Bex or Sur-Bex with Vitamin C.

Each compressed, triple-coated tablet provides six B vitamins. Also, liver fraction and brewer's yeast. Sur-Bex with C adds 150 mg. of ascorbic acid.

No trace of offensive liver odor—only the pleasant aroma of the vanilla-flavored sugar coating. Daily therapeutic dose is one easy-to-swallow tablet. Two or more for severe deficiencies. In bottles of 100, 500 and 1000. Abbott

EACH SUR-BEX TABLET CONTAINS:

Thiamine mononitrate	*6 mg.*
Riboflavin	*6 mg.*
Nicotinamide	*30 mg.*
Pyridoxine hydrochloride	*1 mg.*
Vitamin B_{12} (as vitamin B_{12} concentrate)	*2 mcg.*
Pantothenic acid (as calcium pantothenate)	*10 mg.*
Liver fraction 2, N.F.	*0.3 Gm. (5 grs.)*
Brewer's yeast, dried	*0.15 Gm. (2½ grs.)*

SUR-BEX WITH VITAMIN C contains 150 mg. of ascorbic acid in addition to the vitamin B complex factors.

prescribe

SUR-BEX®

(ABBOTT'S VITAMIN B COMPLEX TABLETS)

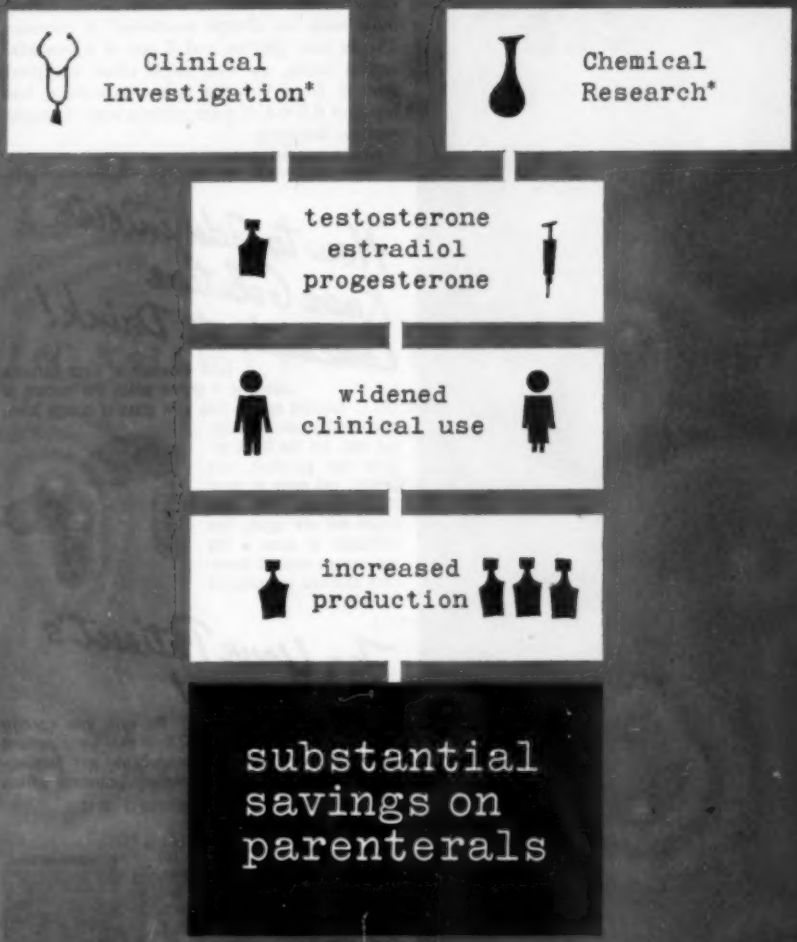
or **SUR-BEX** *with* **C**

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Schering

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*Approximately 430 clinical reports on the use of Schering ethical products were published in scientific periodicals during 1953.

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Good nutrition and good health go hand in hand! Knox Concentrated Gelatine Drink is a worthy protein dietary adjuvant where high protein diet is indicated.

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1. Reich, C., and Mullnos, M. G., Treatment of Refractory Nutritional Anemia with Gelatine. Bull. N. Y. Med. Coll. March 1953.

How to Administer Knox Gelatine Concentrate Drink!

Each envelope of Knox Gelatine contains 7 grams which the patient is directed to pour into a ¾ glass of orange juice, other fruit juices, or water, not iced. Let the liquid absorb the gelatine, stir briskly, and drink at once. If it thickens, add more liquid and stir again. Two envelopes or more a day are average minimal doses. Each envelope contains but 28 calories.



For Your Patient's Protection!

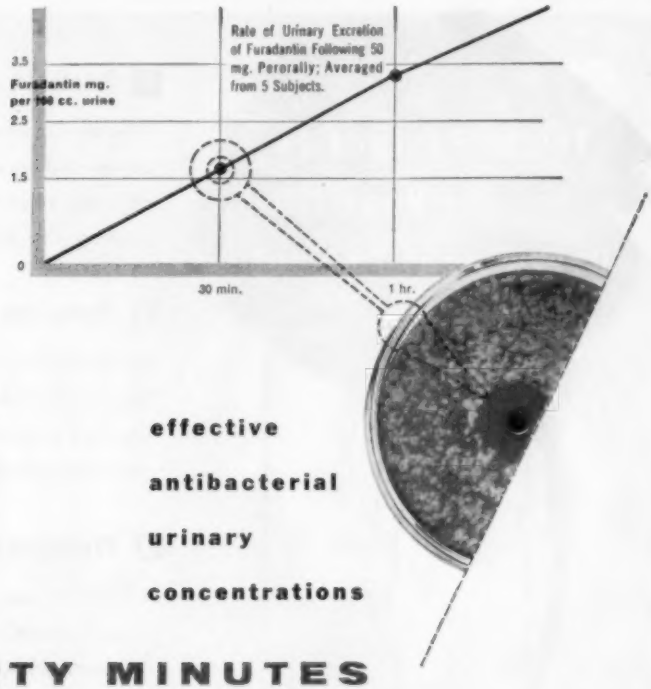
Be sure you specify KNOX so that your patient does not mistakenly get factory-flavored gelatine dessert powders which are 85% sugar.

You are invited to send for brochures on diets of Diabetes, Colitis, Peptic Ulcer . . . Low Salt, Reducing, Liquid, and Soft Diets. KNOX GELATINE, JOHNSTOWN, N. Y. Dept. AIM-2



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ALL PROTEIN • NO SUGAR



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IN THIRTY MINUTES

So remarkable is the affinity of Furadantin for the urinary tract that the urine becomes actively antibacterial within 30 minutes after ingestion, as shown by urinary concentrations and agar plate tests.

Furadantin exhibits an extensive range of antibacterial activity against both gram-positive and gram-negative urinary tract invaders.

Scored tablets of 50 & 100 mg.

IN ACUTE AND CHRONIC URINARY INFECTIONS

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BRAND OF NITROFURANTOIN, EATON

ACCEPTED COUNCIL ON PHARMACY AND CHEMISTRY AMERICAN MEDICAL ASSOCIATION

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1 Protection against hunger pangs

Obocell Complex contains d-Amphetamine and Nicel.* Appetite is curbed *at meals*. Nicel sustains control by extending the effects *between meals*.

2 Protection for his damaged liver

Obocell Complex contains choline,[1] best for transporting neutral fat, and inositol, considered superior in transporting cholesterol.

3 Protection for his enzyme systems

Obocell Complex supplies thiamine, riboflavin and niacinamide in amounts recommended by Zelman.[1] These vitamins are essential in intermediary carbohydrate metabolism and oxidative processes.

1. Zelman, S.: Arch. Int. Med. 90: 141, 1952.

A NEW PRODUCT ANNOUNCEMENT

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d-Amphetamine Phosphate (dibasic)	5 mg.
Nicel*	100 mg.
Choline Bitartrate	200 mg.
Inositol	60 mg.
Thiamine Mononitrate	0.8 mg.
Riboflavin	1.2 mg.
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Offers significant advantages in treating rheumatoid arthritis

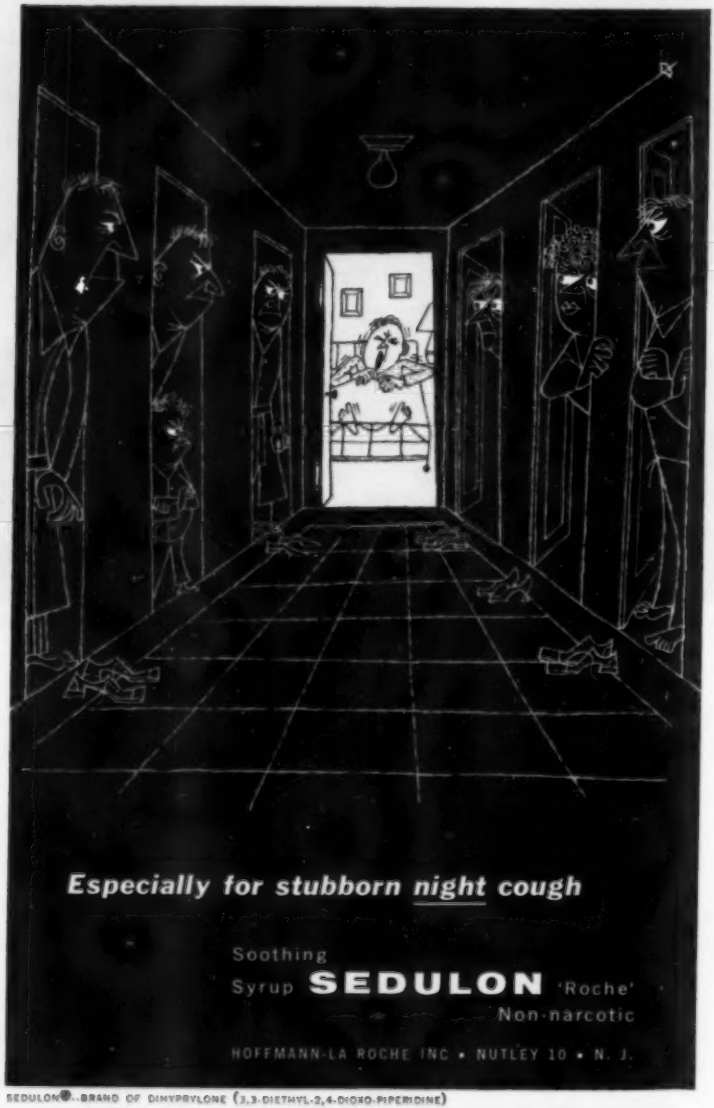
Hydrocortone®

(HYDROCORTISONE, MERCK)

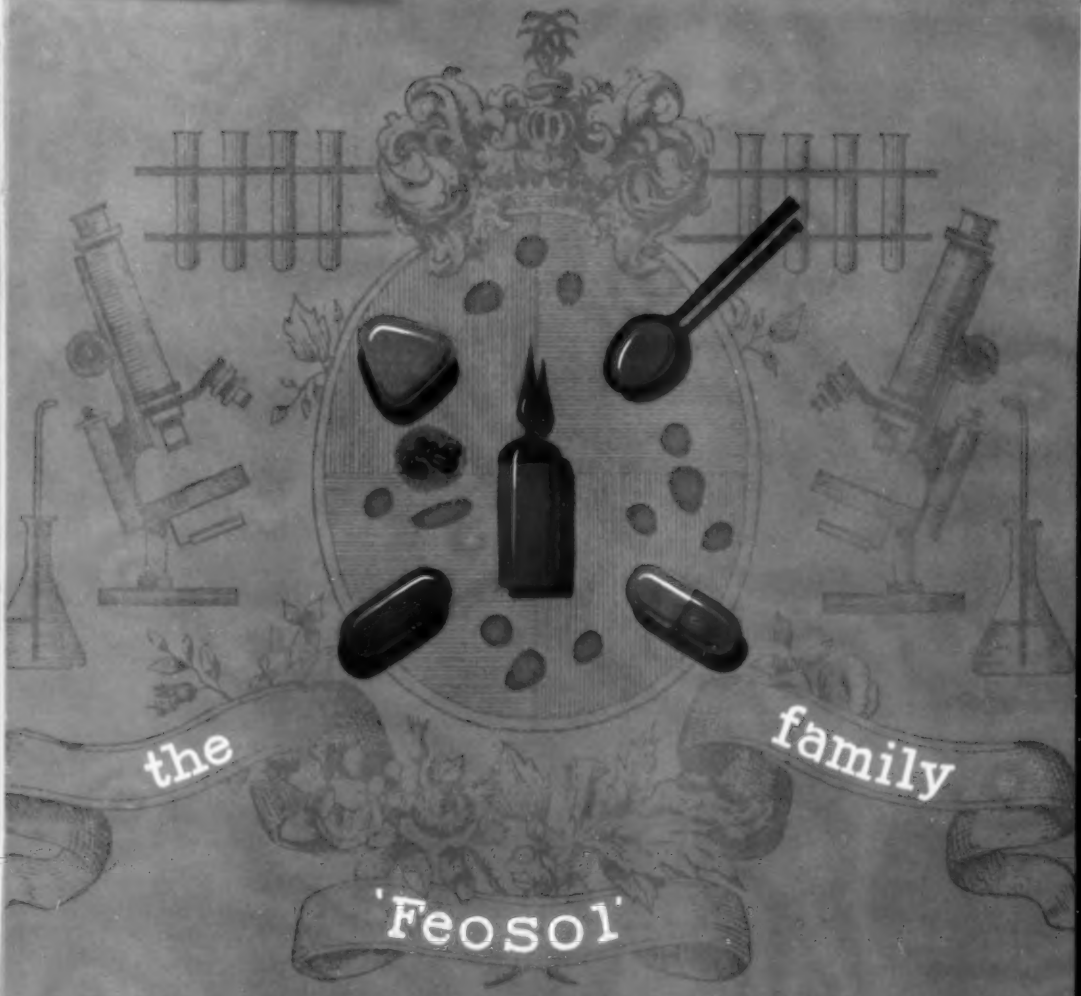
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SUPPLIED: ORAL—HYDROCORTONE Tablets: 20 mg., bottles of 25 tablets; 10 mg., bottles of 50 tablets; 5 mg., bottles of 50 tablets.

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'FEOSOL HEMATONIC'

for the treatment of microcytic and most macrocytic anemias. The recommended daily dosage (3 tablets) delivers: ferrous sulfate, exsiccated, 600 mg.; vitamin B_{12} (Activity Equiv.), 36 mcg.; gastric substance, containing intrinsic factor, 300 mg.; folic acid, 3 mg.; and ascorbic acid, 150 mg.

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for iron-deficiency anemias of infancy and childhood, and for adults who prefer a palatable liquid medication. May also be employed as a light, easily tolerated iron tonic for convalescents or the aged. Two teaspoonfuls provide 5 gr. of ferrous sulfate.

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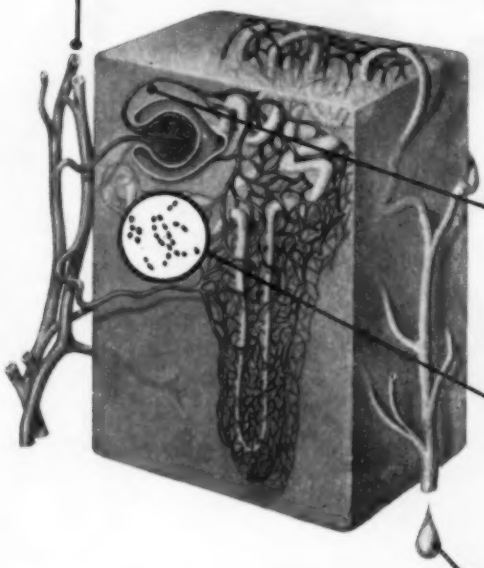
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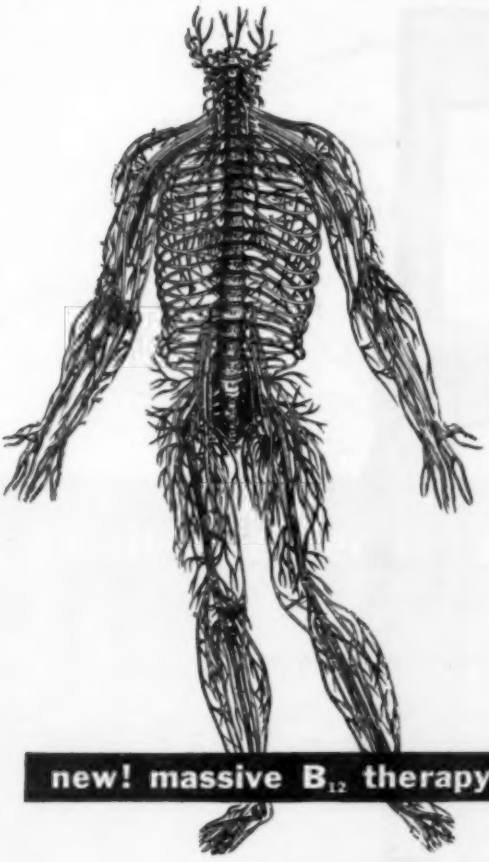
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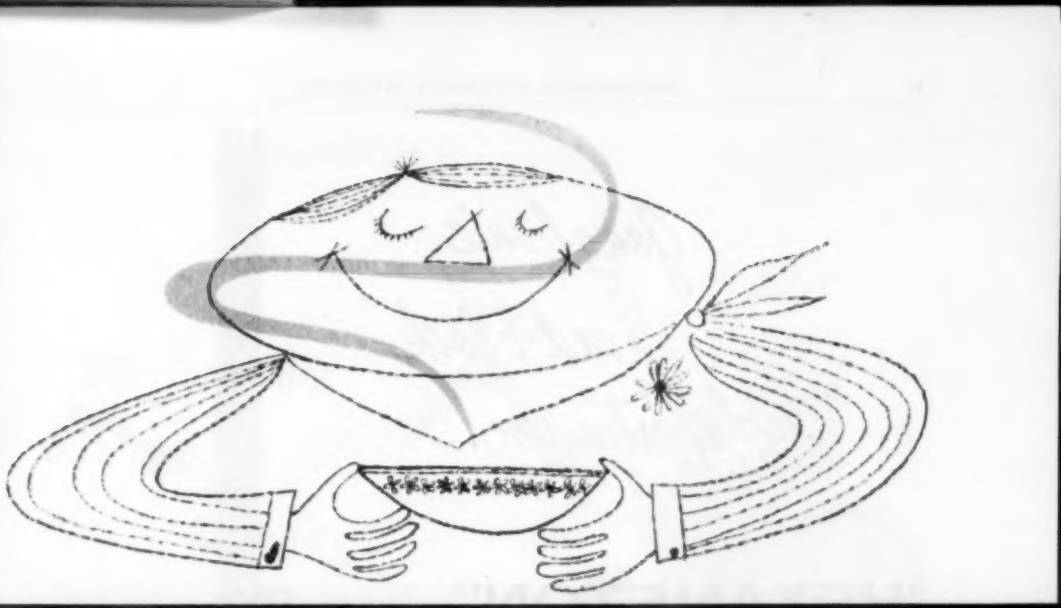
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. . . a well-proven *powerful* hypotensive agent—for use in certain types of hypertension and peripheral vascular disease

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Only an *accurate* electrocardiogram will provide the physician or cardiologist with the true information that he seeks. And from the abnormalities of a 'cardiogram the abnormalities of the corresponding portions of the heart can be read. Likewise Viso records present a 'cardiographic pattern which mirrors the true worth of the instrument.

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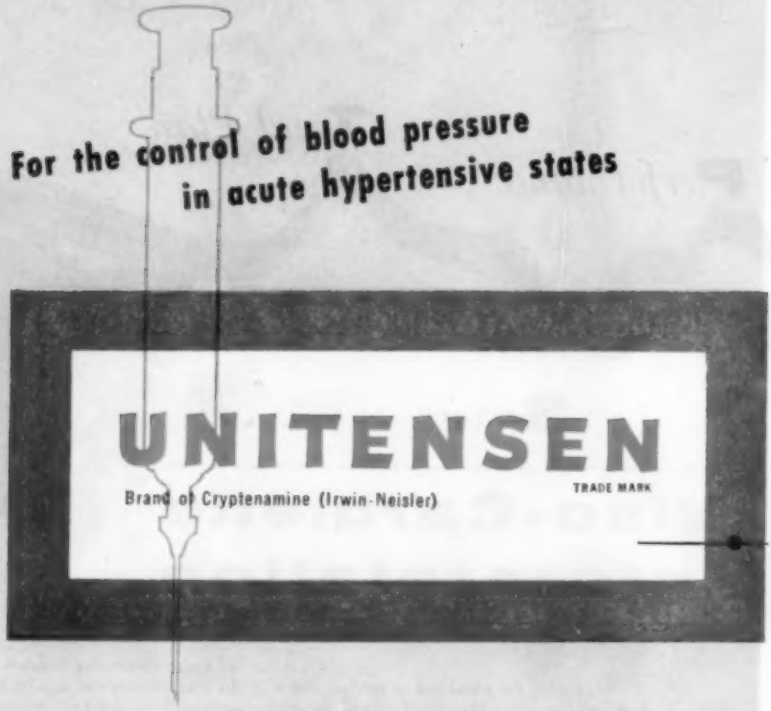
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For the control of blood pressure in acute hypertensive states

UNITENSEN

TRADE MARK

Brand of Cryptenamine (Irwin-Neisler)

in eclampsia and hypertensive crisis

Unitensen combines outstanding efficacy with unequaled safety and has shown remarkable results in a number of serious hypertensive conditions. It is a lifesaving measure in hypertensive crisis. Consistently good results give Unitensen a prominent position in the management of eclampsia, preeclampsia, and preeclampsia with underlying hypertension. [1,2,3]

1. Assali, N. S., and Kaplan, S. A.: S.G.&O. 97, 4: 501-507, 1953.
2. Finnerty, F. A., and Fuchs, G. J., Jr.: Am. J. Obst. & Gynec. 66, 4: 830-841, 1953.
3. Finnerty, F. A.: J. Proc. Soc. Exper. Med. & Biol., to be published.

UNIQUE ADVANTAGES OF UNITENSEN

- Of all the known Veratrum alkaloids or Veratrum alkaloid preparations, Unitensen, brand of cryptenamine, is the only one which is double-assayed for a consistent 4:1 ratio between the dose which produces the side effect of vomiting and the dosage level required for hypotensive action.
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THE ONLY Veratrum PREPARATION

Assayed for therapeutic effect

Unitensen is assayed in dogs for its effects on blood pressure. The C.S.R.* method is used. In contrast to most bio-assay methods, the C.S.R. assay is not based upon a comparison with a known reference standard, since the C.S.R. end-point serves as an absolute measure of hypotensive potency.

*Carotid Sinus Reflex

Assayed for side effect

The emetic dose of Unitensen is determined in animals. For example, a dose of 0.0075-0.008 mg./kilogram of cryptenamine will lower the blood pressure and block the carotid sinus reflex, whereas 0.03 mg./kilogram is necessary to induce vomiting.

Unitensen (Aqueous) is available at present as a parenteral preparation, containing 2 mg. (200 C.S.R. Units) of Cryptenamine per cc. in 5 cc. multiple dose vials.

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an effective, proven plasma volume expander for use in the treatment of shock

Gentran is a clinically effective and notably safe plasma volume expander designed for the prevention and treatment of shock due to hemorrhage, burns, surgical procedures, and other conditions. Prepared for intravenous infusion, it is a sterile, nonpyrogenic 6% w/v solution of dextran in saline.

. . . does not interfere with typing or cross-matching . . . requires no refrigeration . . . is liquid at ordinary temperatures . . . available to your hospital . . . 500 cc. containers . . . easily administered with standard Plexitron solution set . . .

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BRAND OF OXYTETRACYCLINE

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in the treatment of a wide range of infections due to gram-positive and gram-negative bacteria, spirochetes, rickettsiae, certain large viruses and protozoa.

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rapid absorption — Within an hour after oral administration in fasting or non-fasting state, effective serum concentrations of Terramycin may be attained.[1] It is widely distributed in body fluids, organs and tissues and diffuses readily through the placental membrane.[2, 3] Immediate evidence of Terramycin's efficacy is often obtained by the rapid return of temperature to normal.[4] Widely used among patients of all ages, this tested broad-spectrum antibiotic is well tolerated,[5] often when other antibiotics are not.[6]

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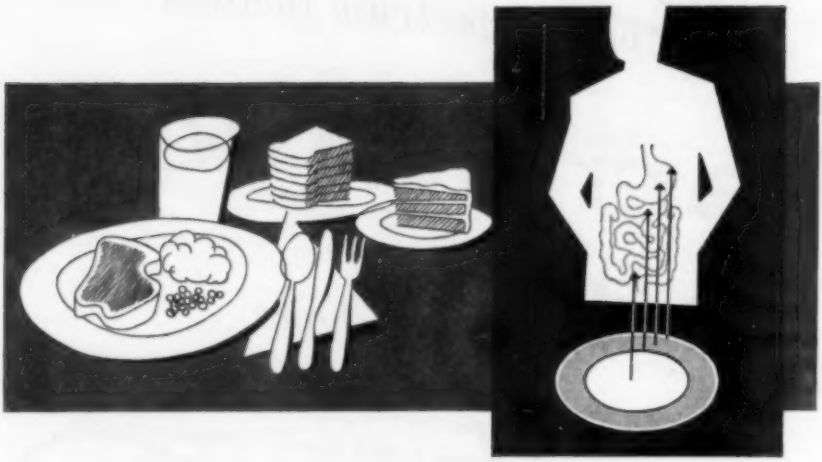
excellent toleration

1. Sayer, R. J., et al.: Am. J. M. Sc. 221:256 (Mar.) 1951.
2. Welch, H.: Ann. New York Acad. Sc. 53:253 (Sept.) 1950.
3. Werner, C. A., et al.: Proc. Soc. Exper. Biol. & Med. 74:261 (June) 1950.
4. Wolman, B., et al.: Brit. M. J. 1:419 (Feb. 23) 1952.
5. Potterfield, T. G., et al.: J. Philadelphia Gen. Hosp. 2:6 (Jan.) 1951.
6. King, E. Q., et al.: J. A. M. A. 143:1 (May 6) 1950.

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effective aid to digestion
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digestant tablets

Special layered construction ensures separately timed action of essential digestants for maximum therapeutic effect

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Pancreatin . . . . . 62.5 mg.
(Equiv. 250 mg. U.S.P.)
Desoxycholic Acid . . . . 50.0 mg.
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DOSAGE: 2 tablets with or just after meals; clinical experience has shown that dose may be reduced, usually after first week, at physician's discretion.

Convertin aids protein digestion through the release of HCl from betaine hydrochloride and through the subsequent action of the pancreatic enzyme, trypsin.

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First, under tongue for quick asthma relief

from aludrine (Isopropyl arterenol) HCl in coating

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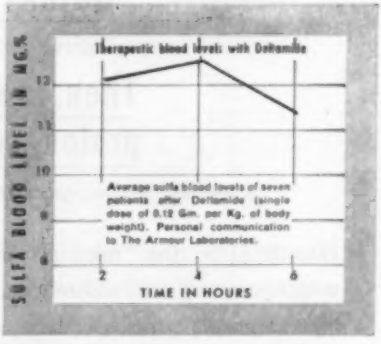
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NEPHENALIN, the "relay-action" tablet combining two widely prescribed, complementary anti-asthmatics, is now available in two potencies: the familiar square, *purple* tablet for adults, and the smaller square, *red* tablet for children. Since a single NEPHENALIN tablet provides quick asthma relief, thereby often replacing the nebulizer, and since relief lasts about four hours, many asthmatic patients will find it the most convenient and efficient anti-asthmatic they have ever used. Bottles of 20 and 100 tablets.

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Sulfadiazine	0.167 Gm.
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Sulfamethazine	0.056 Gm.
Sulfacetamide	0.111 Gm.
Potassium Penicillin G (Buffered)	250,000 units

Tablets: Bottles of 36 and 100.
Powder for Suspension: 60 cc. bottles to provide 2 oz. of suspension by the addition of 40 cc. of water.

DELTAMIDE

the new fourth dimension in sulfa therapy

Each tablet, or each teaspoonful (5 cc.) of pleasant, chocolate-flavored suspension, provides:

Sulfadiazine	0.167 Gm.	Sulfamethazine	0.056 Gm.
Sulfamerazine	0.167 Gm.	Sulfacetamide	0.111 Gm.

Tablets: Bottles of 100 and 1000. **Suspension:** Bottles of 4 oz. and 16 oz.

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***SYRUP OF 'ANTEPAR'** Citrate brand Piperazine Citrate, containing the equivalent of 100 mg. piperazine hexahydrate per cc.

Bottles of 4 fluid ounces and 1 pint

References: 1. Stoll, N. R.: J. Parasitol. *33:* 1, 1947. 2. Bumbalo, T. S., and Gustina, F. J.: To be published. 3. White, R. H. R., and Standen, O. D.: Brit. M. J. *2:* 765, 1953.

Full information sent on request.

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PROTEIN ANABOLIC STEROID HORMONE COMBINATION

...tired elderly patients

With Combandrin, the tired, elderly patient lacking the metabolic support supplied in earlier years by gonadal hormones can often be made stronger, more alert. Formation and retention of protein are promoted, aging bone can be given a "new lease" on life, and mental and emotional reactions may be favorably influenced. More persons can "live"—not merely exist—in their sixties, seventies and eighties. For, the overall results of Combandrin therapy (balanced androgen-estrogen steroid therapy) in the aged "is a lessening of the degenerative state . . ."

Kountz, W. B.: Ann. Int. Med. *35*:1055, 1951.

SUPPLIED: Each cc. contains 1 mg. estradiol benzoate and 20 mg. testosterone propionate in sesame oil, for intramuscular injection. In single-dose disposable Steraject® cartridges and in 10 cc. multiple-dose vials.

Also, Combandrets® — androgen-estrogen combination in convenient tablet form for absorption by transmucosal route.

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for specific and potent
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BUTAZOLIDIN®

(brand of phenylbutazone)

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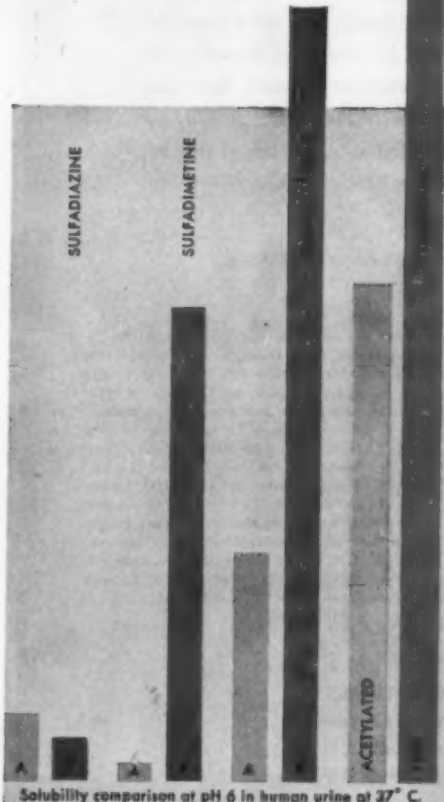
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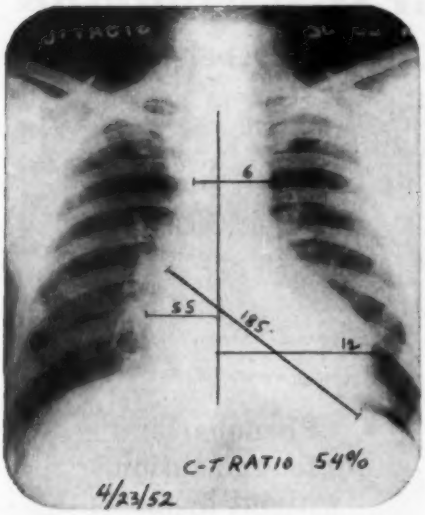
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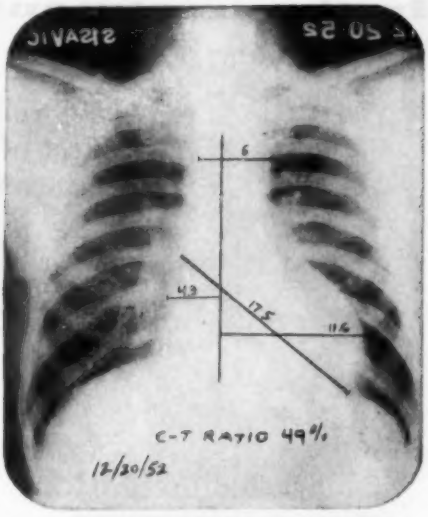
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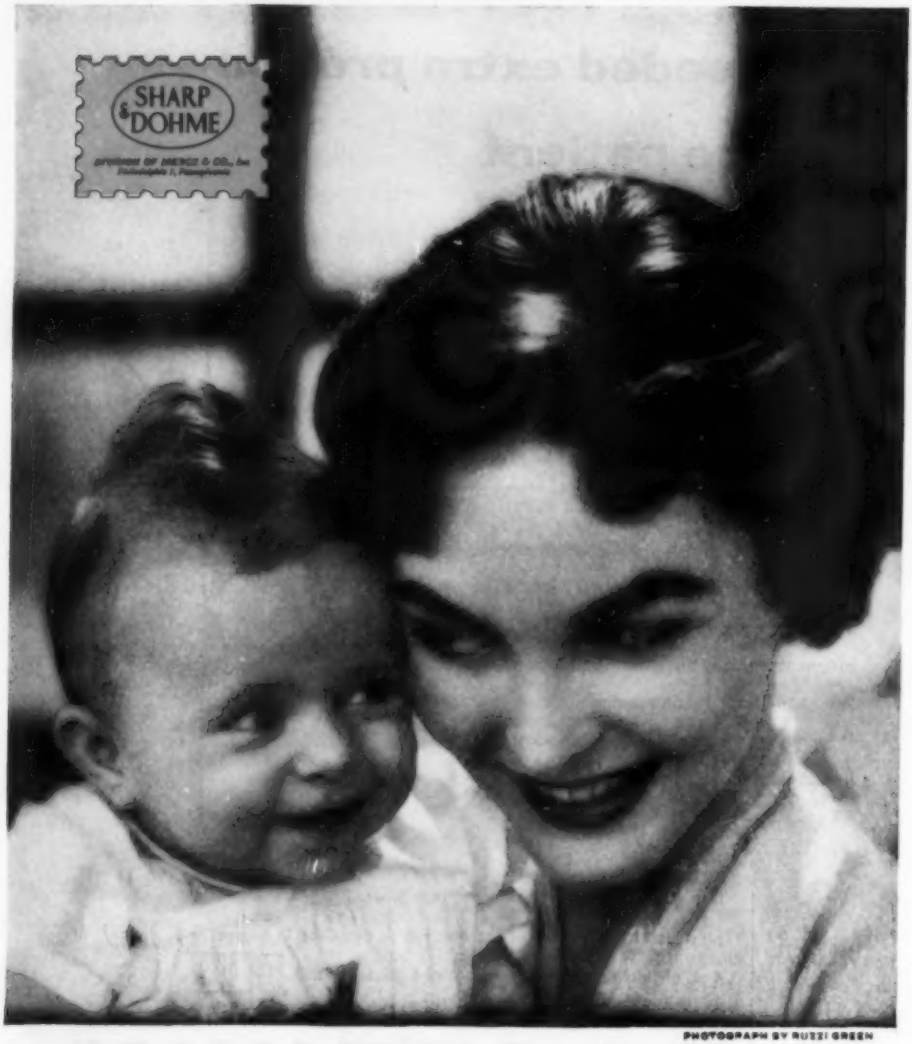


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ANNALS OF
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VOLUME 40 FEBRUARY, 1954 NUMBER 2

EXPERIENCES WITH HISTOPLASMOSIS *

By JOHN A. PRIOR, M.D., F.A.C.P., SAMUEL SASLAW, M.D., Ph.D., and CLARENCE R. COLE, D.V.M., *Columbus, Ohio*

HISTOPLASMOSIS, which previously had been considered to be a rare and fatal disease, is not now of infrequent occurrence especially in the middle western United States. It has been shown that the endemic center of histoplasmosis coincides with the region of high incidence of (1) pulmonary calcifications,[1] and (2) histoplasmin skin reactors.[2] Our studies in Ohio [3, 4, 5] have shown that within the state there is a definite pattern for proved cases of histoplasmosis that coincides with the distribution of histoplasmin reactors and pulmonary calcifications. This demonstrated correlation of skin test, pulmonary calcifications and proved cases suggests that the histoplasmin skin test, even though it may have cross reactions with other fungi, is usually indicative of past or present, clinical or subclinical infection with *Histoplasma capsulatum*.

Studies of clinical histoplasmosis reveal that there tends to be a greater incidence of the disease in the extremes of life.[6] Although the sex distribution is approximately equal among infants and children, the male is more frequently involved after 10 years of age.[6] Accumulated data confirm the growing concept that histoplasmosis is not universally fatal.[5, 7, 8, 9] In fact, the increasing number of cases, reported and unreported, in which the patients recover suggests that it may well be a common infection with relatively few fatalities.

Histoplasmosis is characterized by protean manifestations. They may include irregular fever, weight loss, cachexia, anorexia, nausea, "indigestion," vomiting, diarrhea, jaundice, cutaneous or mucosal ulcerations, cough, sputum, pneumonia that is refractory to all antibiotics, hepatomegaly that

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From the Departments of Medicine and Veterinary Pathology, Ohio State University, Columbus, Ohio.

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occasionally is accompanied by jaundice, splenomegaly and lymphadenopathy. Leukopenia and anemia are common in the more advanced disease. The course may vary from a mild vague illness lasting a few days or weeks to a very fulminating, rapidly fatal disease. Thus, in the usual absence of pathognomonic signs and symptoms, the detection of histoplasmosis requires, first, a high index of suspicion, and second, a specific program of clinical and laboratory study.

It is the purpose of this publication to report, in part, the results of the coöperative studies of the Departments of Medicine and Veterinary Pathology, Ohio State University, on clinical histoplasmosis in man, as well as spontaneous and experimental disease in dogs.

Clinical Aspects in Humans

The following four previously unreported patients, proved by culture and/or biopsy, are presented to illustrate the wide variation in the clinical manifestations of patients ill with histoplasmosis. Three other patients, also unreported, in whom the diagnosis was established by serologic tests, are representative of milder forms of the disease.

Case Reports

Case 1. A 26 year old housewife was near term of a normal pregnancy. On September 18, 1947, 10 days before her admission to the hospital, she noted mild sore throat and cough accompanied by chills and fever. Although she tried the usual home remedies for a "cold" she slowly became more ill, with a harsh, nonproductive cough, chills, sweats and fever ranging from 100° to 103° F.

On September 28 she was admitted in labor to St. Ann's Hospital, Columbus, Ohio, and delivered a normal full term infant. The significant physical findings were pneumonic consolidation over both lower lobes posteriorly and a moderately tender liver palpated 2 cm. below the right costal margin.

Since urinalysis showed the presence of 25 neutrophils per high power field, and acute pyelonephritis was suspected by her attending physicians, penicillin and sulfadiazine therapy was instituted. Two urine cultures were negative.

She continued to have severe shaking chills, profuse sweats, exhaustion and severe nonproductive cough. Later she developed dyspnea, soon followed by cyanosis. Her temperature ranged from 101° to 105.4° F. On the fifth hospital day the icterus index was 6.3; erythrocytes, 4,390,000 (after the patient had received 1,000 c.c. of whole blood); hemoglobin, 10.9 gm.; leukocytes, 8,300, of which 75 per cent were neutrophils, 22 per cent lymphocytes and 3 per cent monocytes. Chest roentgenogram taken on the same day showed marked bilateral basal pneumonia (figure 1A). On the eighth hospital day total serum protein, albumin, globulin, blood urea nitrogen, plasma chlorides and carbon dioxide combining power were all within normal limits. Her course was continuously downhill, with cough productive of small amounts of mucoid sputum, low grade fever and severe dyspnea. On the twelfth hospital day two blood cultures showed no growth after 96 hours' incubation. Intravenous pyelograms revealed no abnormality of the urinary tract. Nonprotein nitrogen was 35 mg. per cent. The blood count was unchanged. On the fourteenth hospital day agglutinations for typhoid fever, paratyphoid fever A and B, brucellosis and heterophil antibodies were all negative. Another blood count showed only the moderate anemia previously

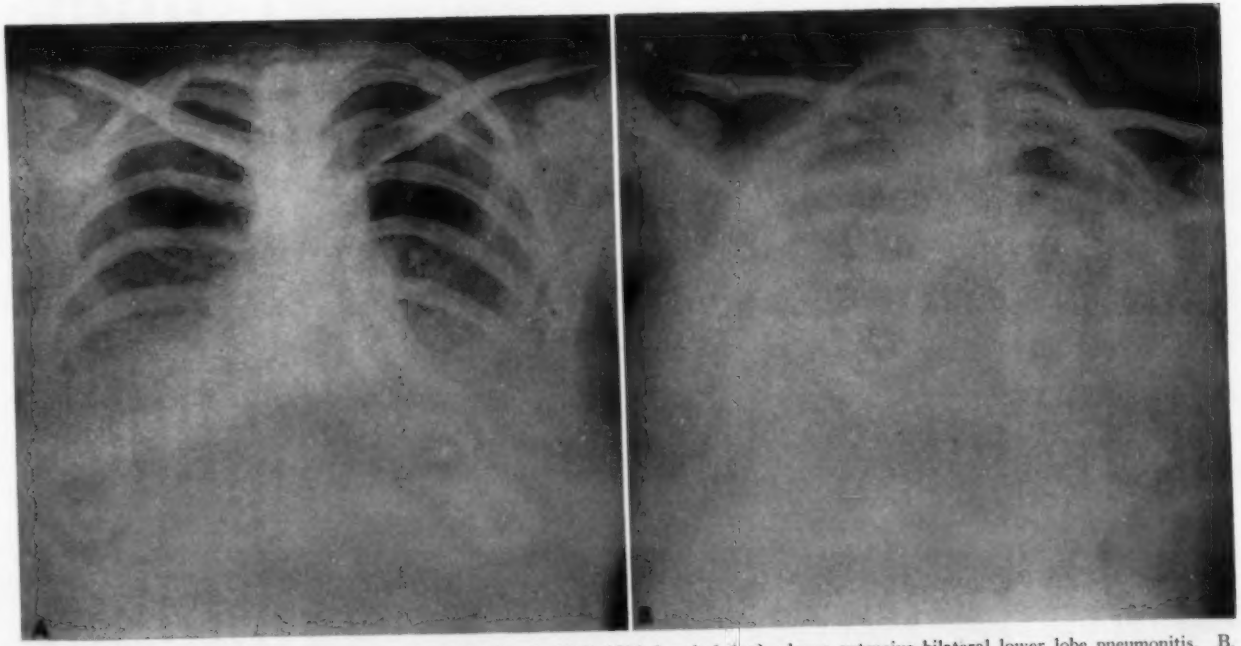


FIG. 1. *Case 1.* A. Chest roentgenogram taken October 3, 1947 (fifth hospital day), shows extensive bilateral lower lobe pneumonitis. B. Chest film taken 12 days later (three days before death) shows marked progression of the extensive bilateral pulmonary pneumonitis.

noted and 4,050 white blood cells, with 81 per cent neutrophils, 16 per cent lymphocytes and 3 per cent monocytes.

Although the patient's temperature had returned to normal by the seventeenth hospital day, the dyspnea and cyanosis became more marked and were not relieved by continuous oxygen administration. Chest x-ray showed marked progression of the pneumonic infiltration, so that only the superior portion of the upper lobes was spared (figure 1B). A thoracentesis was attempted on the right on the nineteenth day but no fluid could be aspirated. She died the following day.

Postmortem examination was conducted at Mt. Carmel Hospital by Dr. Horace Davidson on October 18, 1947. Approximately 500 c.c. of serosanguineous fluid were found in each pleural space. The lungs were heavy, gray and densely consolidated. On cut section the surface was a homogeneous gray, and only a little frothy material could be expressed. The right auricle and ventricle were dilated. The liver and spleen weighed 2,400 gm. and 400 gm., respectively.

Histopathologic Study: In the lungs, eosinophilic material was seen free in the alveoli or adherent to the alveolar walls. The alveoli were filled with numerous macrophages containing many minute round or oval organisms. Many similar organisms were found in the walls of the alveoli. Each was composed of a dark central mass surrounded by a very pale pink or clear zone. The spleen contained one area of circumscribed caseous necrosis surrounded by proliferating fibroblasts, but no microörganisms were found. The adrenals and kidneys showed only nonspecific degeneration. Dilated sinusoids with shrinkage of hepatic cells were seen in the liver. The uterus revealed evidence of recent parturition. The normal architecture of the lymph nodes was disrupted and replaced by diffuse proliferation of reticulum cells and macrophages. Many macrophages were filled with multiple microörganisms similar to those described in the lungs and were morphologically typical of *H. capsulatum.*

Final diagnoses: (1) Histoplasmosis of the lungs and lymph nodes; (2) toxic splenomegaly; (3) parenchymatous degeneration of adrenals, liver and kidneys; and (4) dilatation of right auricle and ventricle.

This patient represents an unusual fulminating pneumonic form of histoplasmosis in which the diagnosis was not established until after necropsy. She had rapidly progressive disease that did not respond to treatment and remained a diagnostic problem throughout the course of her illness.

Case 2. A 20 year old white female first noted during the fall of 1946 that she could not "breathe easily" on exertion. The dyspnea slowly increased and after several weeks she developed low grade fever, constant fatigue, cough and pleuritic pain on the right. A diagnosis of "virus pneumonia" was made and she was treated with penicillin, but all symptoms persisted. She was studied subsequently by several other physicians and at a tuberculosis clinic. Although a definite diagnosis was not made, she was given streptomycin and penicillin, without benefit.

In June, 1947, bronchoscopic examination by Dr. Karl Klassen at White Cross Hospital, Columbus, Ohio, revealed marked hyperemia of the right lower bronchus, with some blood and purulent exudate seen welling up in the bronchus. Fungus cultures of the bronchial aspirate showed the presence of *H. capsulatum,* and a diagnosis of pulmonary histoplasmosis was made. Chest roentgenogram showed marked bilateral hilar enlargement, with infiltration extending into both lungs, and atelectasis of the middle lobe (figure 2). She was kept at moderate rest without other therapy during the entire summer, with considerable improvement, and she was able to return to college in September, 1947.

She was admitted to the University Hospital on February 27, 1948, because of continued cough, expectoration and fatigue. Physical examination revealed no abnormality except in the right lung, where percussion was impaired over the right middle and lower lobes and breath sounds were wheezing over the same area.

Bronchoscopy on February 28 revealed the mucous membranes of the right middle lobe to be intensely inflamed and thickened. Just below the right upper lobe orifice, which appeared to be normal, there was marked narrowing of the right bronchus to 2 or 3 mm. in diameter, and a small amount of blood was seen coming through the stenotic area.

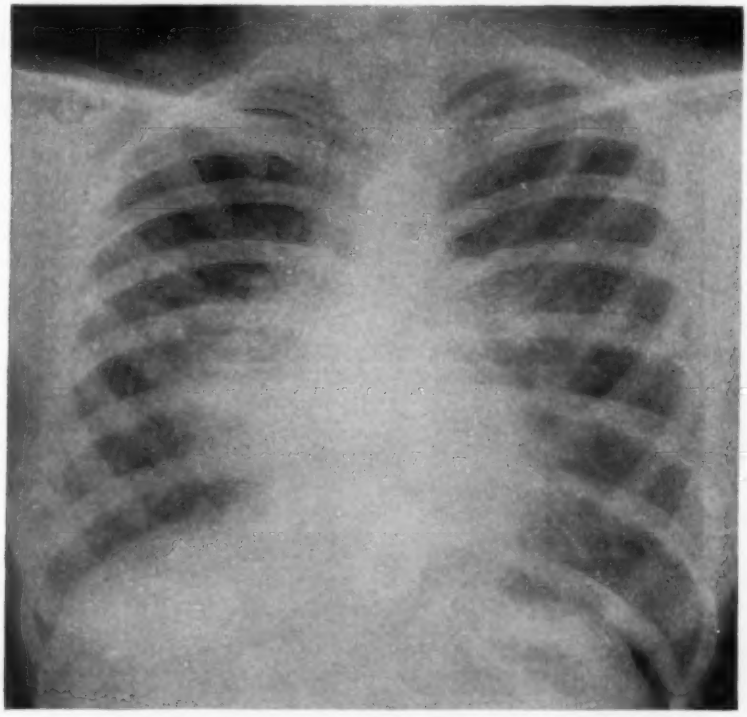


FIG. 2. *Case 2.* Chest roentgenogram taken June, 1947, shows marked bilateral hilar lymphadenopathy with infiltration extending into both lungs and atelectasis of middle lobe.

Tuberculin skin tests (PPD 1 and 2) were negative. Histoplasmin skin test was positive. Histoplasmosis complement fixation titer was 1 : 20. Repeated cultures of sputum and bronchial aspirate were negative for fungi or tubercle bacilli. Complete blood count and urinalysis were not remarkable.

Chest roentgenogram taken on March 1, 1948 revealed considerable hilar enlargement on the right, with surrounding pneumonic infiltrate (figure 3A). Bronchograms made the same day showed narrowing of the right upper lobe bronchus and compression of the middle and lower lobe bronchi (figure 3B). The extrinsic pressure had not completely occluded any bronchus.

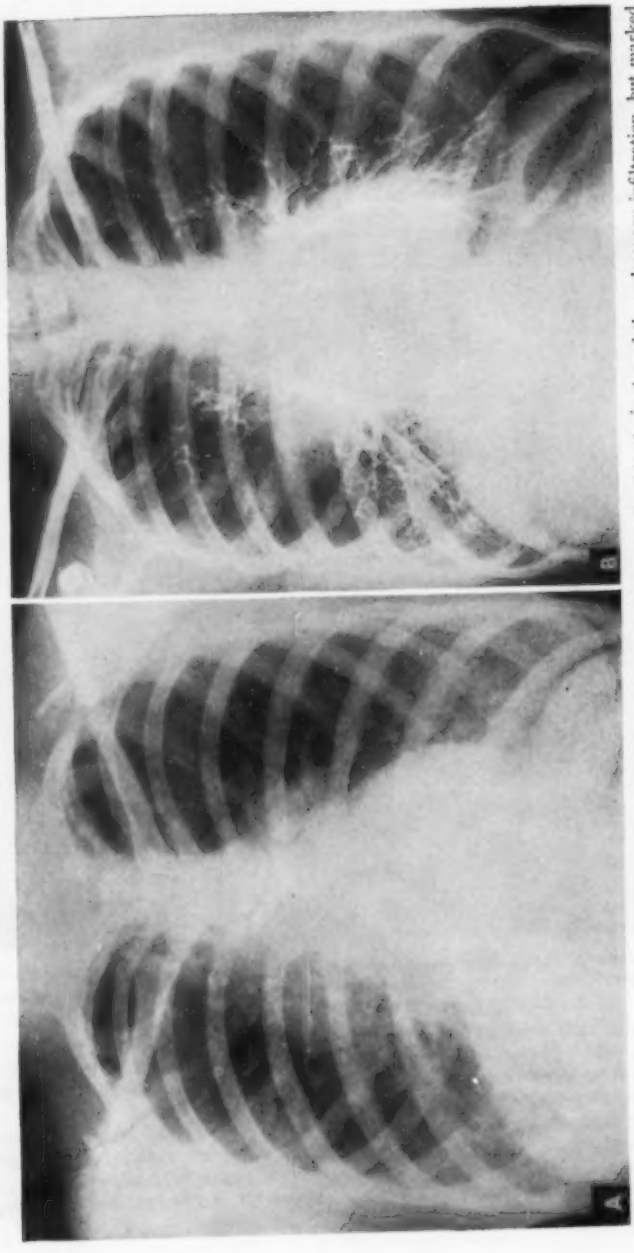


FIG. 3. *Case 2.* A. Chest roentgenogram taken March 1, 1948, shows considerable absorption of the pulmonary infiltration, but marked hilar lymph node enlargement remains on the right, with some atelectasis and infiltration at the base and midlung. B. Bronchiogram performed the same day reveals marked narrowing of the right upper lobe bronchus and compression of the middle and lower lobe bronchi.

She had been slowly improving, and on August 23, 1948 physical and bronchoscopic examination was unchanged from the previous admission. Repeat studies of sputum and bronchial aspirate did not show any fungi or tubercle bacilli. Histoplasmosis complement fixation titer was 1:10. Blood count showed only mild hypochromic anemia. Phenolsulfonphthalein and bromsulfalein excretion tests, blood urea nitrogen and the urinalysis were all negative.

She was admitted for the third time on June 28, 1949. She had been feeling well except for easy fatigability, cough productive of 3 or 4 ounces of whitish sputum per day, occasional hemoptysis and frequent wheezing. Bronchography revealed no significant change except for slightly more bronchial stenosis.

Since the above hospital study she has done quite well. At present she is married, and is able to do her housework without undue fatigue. She still has considerable wheezing, made worse by exertion, and cough productive of moderate amounts of whitish sputum, especially on arising in the morning. Chest roentgenograms on December 30, 1952, show persistent hilar swelling on the right.

This is an example of nonfatal pulmonary histoplasmosis characterized by fever, fatigue, cough, wheezing, pleuritic pain and exertional dyspnea, with marked bilateral hilar lymphadenopathy and pulmonary infiltration. The diagnosis was established only by an intensive search for the causative agent. The patient recovered from the acute illness. Her present complaints are the sequelae of the bronchial obstruction caused by extrinsic pressure from the peribronchial nodes.

Case 3. A 60 year old white male laborer was admitted to the University Hospital on March 23, 1951, with a chief complaint of persistent sore throat, which had been present for three months. He had lost 30 pounds in weight, which he attributed to decreased food intake as a result of dysphagia. Three weeks before admission he noted an ulcer at the base of his tongue and consulted a physician for the first time. A biopsy of the ulcer was performed by Dr. John Dole, Ironton, Ohio, and a diagnosis of histoplasmosis was made from the histopathologic study.

When he was referred to the University Hospital, examination revealed a poorly nourished 60 year old man who appeared chronically ill. Temperature, 98.8° F.; pulse, 80; respirations, 16; blood pressure, 126/80 mm. of Hg. The significant findings were: (1) There was a deep ulcer on the posterior one third of the tongue measuring 2 cm. in diameter, the margin of which was elevated above the surface and the base covered with gray necrotic material (figure 4). (2) The left anterior faucial pillar was occupied by a superficial ulcer covered with gray, friable exudate, measuring 1.0 by 1.5 cm. (3) Two other small superficial ulcerations were seen on the posterior pharyngeal wall. (4) Hard, discrete cervical, axillary and inguinal nodes were palpated. (5) The liver was firm, nontender, and enlarged to 12 cm. below the costal margin.

Laboratory Data: On admission Wintrobe sedimentation rate (corrected) was 32 mm. in one hour; erythrocytes, 3,520,000; hemoglobin, 10.8 gm.; leukocytes, 9,950 (60 per cent neutrophils, 40 per cent lymphocytes). Histoplasma complement fixation tests taken at weekly intervals varied from 1:1280 to 1:2560. The collodion agglutination titer was 1:20 on admission and 1:80 thereafter. Urinalysis revealed albumin, 40 mg. per cent, and 4 to 6 white blood cells per high power field. Blood urea nitrogen was 62.5 mg. per cent. Total serum protein, 8.65 gm.; albumin 3.83, and globulin, 4.82 gm. Thymol turbidity, 50 units. Cephalin flocculation, 4 plus. Van den Bergh and bromsulfalein excretion were within normal limits. Prothrombin, 60 per cent. Phenolsulfonphthalein excretion was only 15 per cent after two hours.

Repeated blood counts showed no significant alteration in the erythrocytes or hemoglobin content. Leukocytes ranged from 9,000 to 14,850, with 65 to 75 per cent neutrophils and the remainder lymphocytes. Hepatic function studies during the patient's hospital stay showed no change from original determinations. Histoplasmin skin test was negative. Indirect laryngoscopy revealed nodular granulomatous lesions on both vocal cords and a large area of ulceration in the interarytenoid space.

Biopsy of the tongue ulcer (figure 5) showed granulomatous lesions containing many microörganisms morphologically typical of *H. capsulatum*. The lymph node removed from the left axilla showed reticulum cell hyperplasia. *H. capsulatum* was cultured from the lymph node, blood stream and bone marrow.

Chest roentgenogram showed moderate pleural thickening over both apices but no evidence of active disease.



FIG. 4. *Case 3.* Crater-like ulcer 2 cm. in diameter, at base of tongue, which caused persistent discomfort and marked pain on swallowing. Other smaller ulcerations were seen on left anterior faucial pillar and posterior pharyngeal wall.

On the third hospital day the patient was started on Atabrine, 200 mg. three times a day for one week and then twice a day for the next three days, at which time it was discontinued because of nausea. The latter dose was resumed five days later and continued until discharge. Warm saline irrigations to the throat were given four times a day. The patient remained afebrile during his hospital stay, and noted some improvement in his discomfort and dysphagia. Although the large ulcers in the throat looked a little cleaner, there was no appreciable change in size and the patient lost 7 pounds during this time. He was discharged on the thirty-sixth day to be followed by his local physician. He was instructed to continue the Atabrine, 200 mg. twice a day, and to return in one month for study. However, four weeks after returning to his home the patient died unexpectedly. The circumstances of his death are not known, and an autopsy was not performed.

It is of interest to note that, although the patient complained only of his sore throat and tongue, and attributed the weight loss solely to the accom-

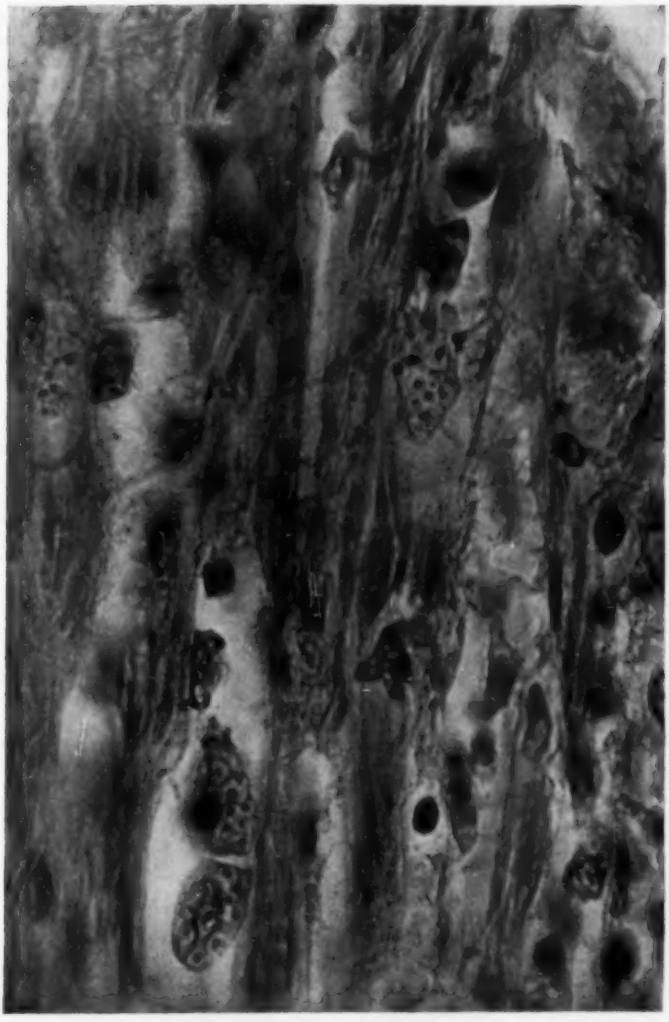


FIG. 5. *Case 3.* Photomicrograph of granulomatous lesion in tongue shows many *H. capsulatum.* (× 1000.)

panying dysphagia, there was evidence of dissemination of the histoplasmosis throughout his body. *H. capsulatum* was cultured from a lymph node, blood and bone marrow, as well as demonstrated microscopically in the tongue. Following the institution of Atabrine therapy, it was not possible after repeated attempts to recover the fungus again.

Case 4. A 75 year white male farmer was admitted to the University Hospital on May 17, 1951, complaining of (1) sore mouth of three months' duration, and (2) urinary frequency, nocturia and hesitancy for 10 years. On several occasions he had had dysuria, which was promptly relieved by treatment prescribed by his physician, who told him he had a "kidney infection." About six months before his admission he experienced generalized malaise and weakness that became progressively more severe. Three months later he noted onset of "sore mouth," which for eight weeks

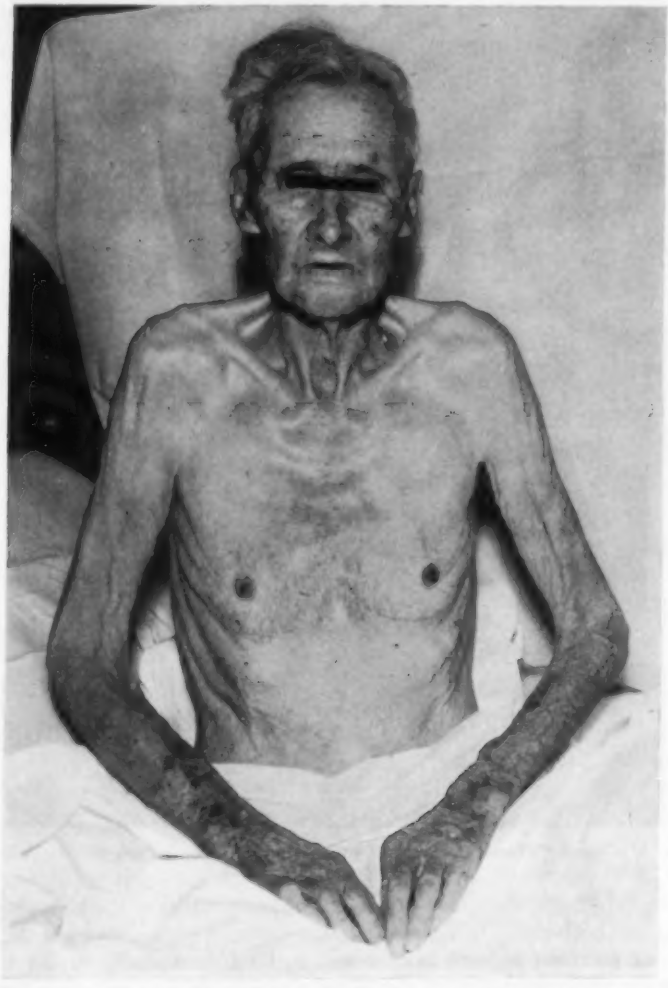


FIG. 6. *Case 4.* Photograph showing pigmentation of face, neck, hands and forearms, as well as the emaciation.

prior to admission had been so severe that eating was virtually impossible and as a result his weight had dropped from 192 to 129 pounds.

On his admission to the Urology Service on May 17 it was felt that, because of his prolonged inability to eat, he was suffering from pellagra in addition to benign prostatic hypertrophy. Consequently, he was given large doses of riboflavin and vitamin B complex. However, during the course of a histoplasma serologic testing program, it was found that he had high titers in both the collodion agglutination and complement fixation tests, and he was transferred to the Medical Service on May 24 with a tentative diagnosis of histoplasmosis.

Physical examination revealed an emaciated male appearing chronically ill; temperature, 98° F.; pulse, 78; respirations, 20; blood pressure, 100/62 mm. of Hg. The skin was dry and scaly, with very poor turgor. Over the face, neck, hands and forearms there was definite brownish pigmentation (figure 6). Several small ragged ulcers were seen over the posterior third of the tongue, left soft palate and left buccal mucosa. Enlarged cervical, axillary and inguinal lymph nodes were palpated. The heart was enlarged to the left, and soft systolic murmurs were heard over the aortic and mitral areas. The liver was felt 2 cm. below the costal margin. The prostate was enlarged and tender.

Initial Laboratory Data: Erythrocytes, 5,500,000; hemoglobin, 15 gm.; leukocytes, 3,200, with 80 per cent neutrophils, 19 per cent lymphocytes and 1 per cent basophils. The urine contained 10 mg. per cent albumin and 5 to 10 white blood cells per high power field. Serum calcium, 3.45 mg. per cent. Alkaline phosphatase, 14.95 units. Acid phosphatase, none. Blood urea nitrogen, 19.5 mg. per cent. Total serum protein, 8.38 gm.; albumin, 2.18 gm.; globulin, 7.2 gm. Van den Bergh, 0.4 direct and 1.05 total. Thymol turbidity, over 100. Cephalin flocculation, 3 plus. Bromsulfalein, 15 per cent retention after 45 minutes. Sugar, potassium, sodium, chloride and prothrombin levels in the blood were all normal. Phenolsulfonphthalein, 13 per cent excretion after two hours. On June 6 the eosinophil count was 156 per cubic millimeter. Serum sodium, 275 mg. per cent; potassium, 17.5 mg. per cent; chlorides, 405 mg. per cent. Chest roentgenogram revealed a very soft diffuse infiltration scattered throughout all lobes (figure 7). Electrocardiogram showed right axis deviation and evidence of myocardial damage. Blood and bone marrow cultures were positive for *H. capsulatum*. Histoplasma collodion agglutination on May 24 was 1:20. The histoplasmin skin test was negative.

Biopsy of a pharyngeal ulcer showed extensive ulceration of the stratified squamous epithelium. The underlying stroma contained many large macrophages and giant cells, with some lymphocytes and plasma cells. Within the cytoplasm of the macrophages were tiny unicellular organisms consisting of round or slightly flattened nucleus-like structures surrounded by a clear ring or capsule. It was the pathologist's conclusion that the tissue showed intracellular organisms morphologically similar to *H. capsulatum*.

Course: Throughout his hospital course he was unable to eat, and he was given intravenous 10 per cent glucose with 5 per cent Amigen and, when he could tolerate a small polyethylene tube, he was given homogenized milk. Because of his persistent dyspnea and cyanosis he was kept in oxygen most of his hospital stay. His course was progressively downward with increasing apathy and weakness. He became incontinent of urine, and an indwelling catheter was inserted. Two days later he began to have fever, ranging from 101° to 103° F. daily, which persisted until his death. Urinalyses revealed many white blood cells, with 10 to 50 mg. per cent of albumin, and cultures were positive for *Staphylococcus aureus, Escherichia coli* and *Aerobacter aerogenes*. He was given sulfonamides, penicillin and Terramycin for his urinary tract infection.

On June 7, after the diagnosis of histoplasmosis had been definitely established, he was given Atabrine, 0.2 gm. twice a day. Histoplasma collodion agglutinations

were 1:80 on May 28, 1:160 on June 1, 1:80 on June 4, 1:80 on June 11, and 1:160 on June 20. The complement fixation tests were 1:80 on four determinations. It is interesting to note that, although repeated cultures were made both ante mortem and post mortem, it was not possible to grow the fungus again after this date. His blood pressure ranged from 94/66 to 82/54 mm. of Hg during his hospitalization, but during the last two days of his life his systolic pressures fell to an average of 78. He died on June 23, his thirty-seventh hospital day.

Necropsy: The heart was extremely soft and flabby, weighing 340 gm. There were large areas of epicardial fibrosis over the anterior surfaces of the left and right ventricles. Coronary arteries showed only minimal atherosclerosis. Except for the

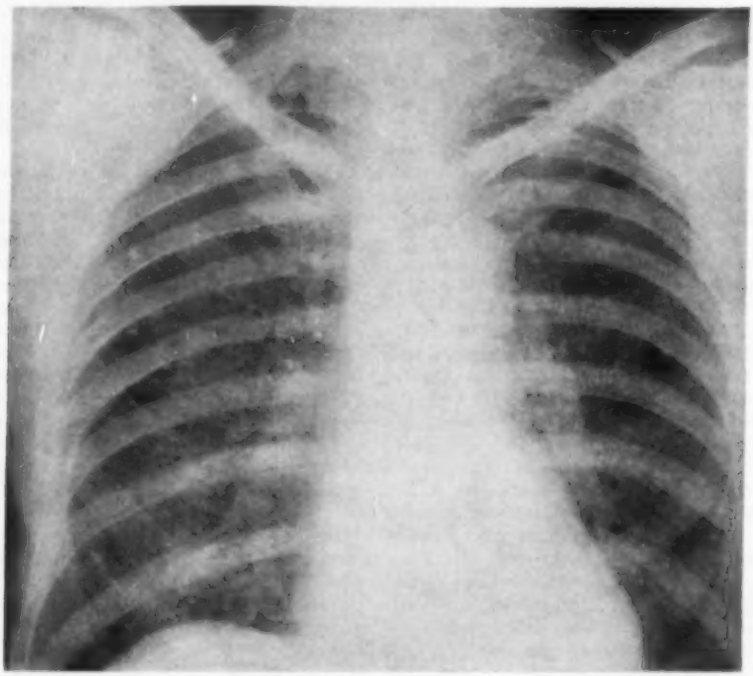


FIG. 7. *Case 4.* Chest roentgenogram shows very fine nodular infiltration throughout both lungs.

posterior portion of both lower lobes, the lungs were crepitant. On section, diffuse emphysema was noted and the dependent portions were markedly congested. Bronchi were patent, although the mucosa was hyperemic and thickened. The spleen weighed 430 gm. and was quite soft. Numerous 1 to 2 mm. nodular areas were seen on the capsule. On section the pulp was mushy, with loss of the normal architecture. In the cecum three areas of ulceration were found, the largest of which measured 1.0 by 1.5 cm. (figure 8). The remainder of the gastrointestinal tract appeared normal. Both adrenals were greatly enlarged, almost to the size of a small lemon. The right weighed 50 gm. and the left 65 gm. On section almost no visible adrenal tissue remained, being replaced by extensive caseous necrosis (figure 9). The right kidney

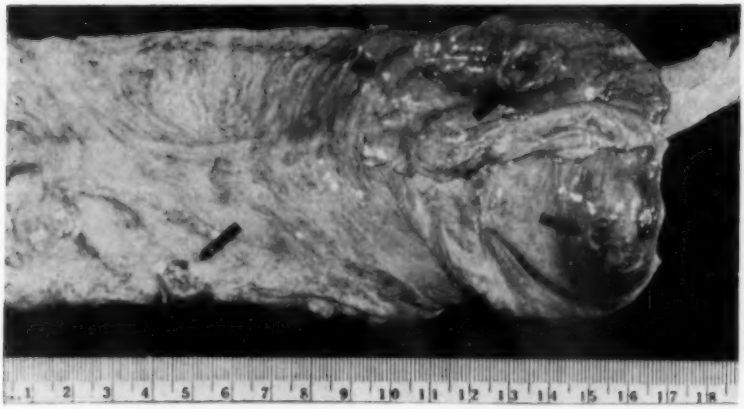


FIG. 8. *Case 4.* Two areas of ulceration may be seen in the head of the cecum, as well as another small ulcer seen along the lower margin of the specimen.

showed severe hydronephrosis, with dilation of the calyces and pelvis to three times normal size. In the medullary portion and occasionally in the cortex, dark gray-yellow linear streaks and tiny punctate areas were seen, suggesting acute pyelonephritis with tiny abscesses. In the left kidney similar changes were noted in the medulla, although there was no dilation of pelvis or calyces. The bladder was distended and the wall was heavily trabeculated with several small diverticula. The



FIG. 9. *Case 4.* Photograph demonstrating the extensive caseous necrosis of the right adrenal. Only a very small amount of adrenal tissue is visible.

mucosa was reddened and a 4 mm. superficial ulceration was seen near the orifice of the left ureter. The prostate was nodular and enlarged to twice normal size.

Histopathology: The heart showed evidence of myocarditis, with scattered granulomatous areas, giant cell formation, arteritis and fibrosis. In the lungs there were many scattered granulomas containing giant and epithelioid cells. Some large mononuclear cells were seen to contain three to eight bodies thought to represent *H. capsulatum.* In addition, there were lobular pneumonia and emphysema. The spleen showed scattered granulomas. In the liver there was chronic hepatitis, with atrophy of liver cells, necrosis, diffuse lymphocytic infiltration, foci of liver cell regeneration and scattered granulomas, an occasional one of which was shown to contain a few organisms morphologically typical of *H. capsulatum.* The adrenals showed massive caseation necrosis. There was nodular hyperplasia, and chronic infection seen in the prostate. The brain showed focal areas of granuloma and encephalomalacia. Granulomatous areas were found in the ulcerations on the palate, and in the mononuclear cells there were a number of intracellular bodies resembling histoplasma. Granulomatous areas were seen in the bladder wall, cecum, kidneys, bone marrow, lymph nodes and liver.

It was the conclusion of the pathologist that this was generalized histoplasmosis, with involvement of lungs, liver, spleen, kidneys, bone marrow, heart, adrenals, palate, cecum, bladder, lymph nodes and brain. These findings, especially the extensive necrosis of the adrenals, confirmed the antemortem diagnosis of histoplasmosis with Addison's disease.

Case 5. A 24 year old Negro male student was admitted to the University Hospital on May 17, 1950, at which time he stated that 10 days before admission he had developed chilly sensations, fever, generalized malaise and a nonproductive cough. He had continued to have daily temperature elevations varying from 100° to 101° F., as well as the other symptoms. Physical examination revealed no detectable abnormality. There was no palpable enlargement of lymph nodes, liver or spleen.

Laboratory Data: Erythrocytes, 4,940,000; hemoglobin, 14.8 gm.; leukocytes, 5,900, of which 38 per cent were neutrophils, 58 per cent lymphocytes and 4 per cent monocytes. Urinalysis was negative. Total serum protein, albumin, globulin, blood urea nitrogen, van den Bergh and fasting blood sugar were normal. Cephalin flocculation, thymol turbidity, heterophil, typhoid, paratyphoid, proteus and brucella agglutinations were all negative. Throat and three blood cultures showed no pathogenic bacteria. Histoplasmin skin test was positive; tuberculin skin tests were negative.

Chest roentgenograms revealed only bilateral hilar and right paratracheal lymphadenopathy (figure 10). No parenchymal lesions were seen. Excretory urograms and upper and lower gastrointestinal x-ray studies were reported as negative. Bone marrow aspiration showed only normal marrow elements. Stool cultures showed no pathogenic organisms, ova or parasites. On May 30, cold and heterophil agglutinations were negative.

The patient's temperature ranged up to 102° or 103° F. each day. On the seventh day he was started on streptomycin, 1.0 gm. per day. After the eighth day his temperature began to fall and remained at normal levels by the eleventh day. He was discharged on the twelfth day, apparently recovered, although no definite diagnosis had been established.

The patient was re-admitted one month later because of return of fever and all of his symptoms. He stated that his temperature had been normal and that he had felt well for one week after return to his home. Then he noted that he had daily temperature elevations from 100° to 102° F. which had persisted up to his re-admission. He had associated malaise, aching and slight cough. Physical examination again did not reveal any significant abnormality.

Laboratory Data: Erythrocytes, 5,060,000; hemoglobin, 14.3 gm.; leukocytes, 15,750, of which 63 per cent were neutrophils, 32 per cent lymphocytes, 1 per cent

monocytes and 4 per cent eosinophils. Urinalysis, thymol turbidity, van den Bergh, total serum protein, globulin, albumin and blood urea nitrogen were within normal limits. Brucella, tularemia, cold and heterophil agglutinations were negative. Throat and stool cultures showed no pathogenic organisms.

Chest roentgenogram showed no significant change in the bilateral hilar and right paratracheal lymphadenopathy. After six days of bed-rest he became afebrile and symptom free, and after four additional days of observation he was discharged. Since his discharge he has been in good health.

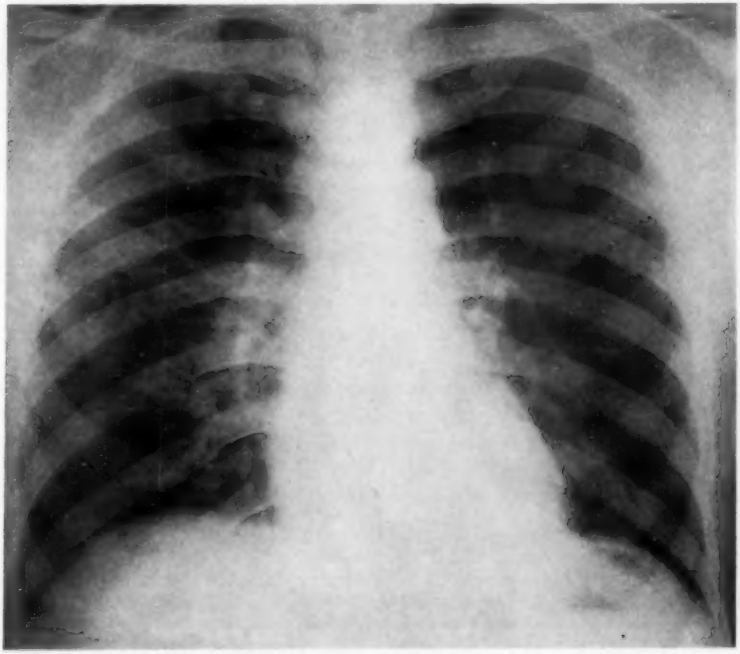


FIG. 10. *Case 5.* Chest roentgenogram taken May 18, 1950, shows enlargement of both hila and a paratracheal lymph node on the right.

Two days after his discharge the histoplasma collodion agglutination test was reported to be positive in a dilution of 1:80 and the complement fixation test was positive in dilution of 1:40. On the basis of this report, the histoplasmin skin reaction, the hilar and paratracheal lymph node enlargement with the vague symptoms, in retrospect a diagnosis of histoplasmosis can be made.

This is an example of a relatively low grade infection with pulmonary lymphadenopathy and only moderate constitutional symptoms.

Case 6. A 31 year old Negro female was admitted to the University Hospital on May 8, 1950, complaining of fever, chills and generalized aching of three days' duration. At the onset there had been considerable serous nasal discharge and some

pharyngitis. In addition she had noted marked anorexia and some oliguria, but no other gastrointestinal or urinary complaints.

Physical Examination: Temperature, 104.4° F.; pulse, 96; respirations, 24; blood pressure, 120/70 mm. of Hg. Inspection revealed a well developed, well nourished Negro female who appeared acutely ill. The only abnormal findings were poor oral hygiene and chronic cervicitis.

Laboratory Data: Erythrocytes, 4,570,000; hemoglobin, 12.6 gm.; leukocytes, 9,900, of which 82 per cent were neutrophils, 14 per cent lymphocytes and 4 per cent monocytes. The urine was essentially normal except for 10 mg. per cent of albumin.

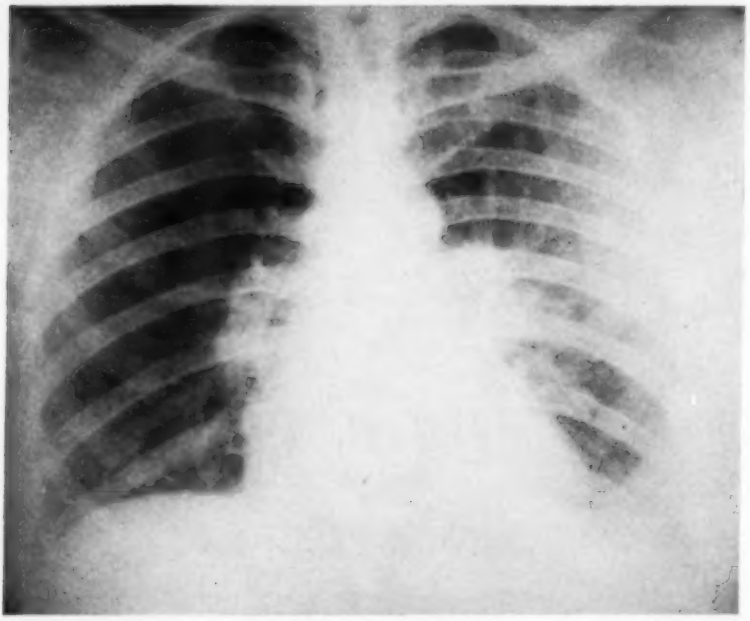


FIG. 11. *Case 6.* Chest roentgenogram taken on fourth hospital day shows bilateral hilar lymphadenopathy, hazy infiltrate in the left midlung radiating from the hilum and some pleural reaction at the left base.

Blood urea nitrogen was 11 mg. per cent. Kahn and VDRL serology were negative. Sedimentation rate was 93 mm. in one hour (Westergren).

Chest roentgenogram showed hazy infiltration in the left midlung field and bilateral hilar lymphadenopathy.

It was the impression that the patient had primary atypical pneumonia, and she was given Aureomycin, 2 gm. per day. Although there was symptomatic improvement, and repeated examinations had not disclosed any other significant findings, her temperature continued to rise each day to 101° to 102° F. Consequently, after one week Aureomycin was discontinued.

On the third hospital day repeat blood count was essentially the same as on admission. Blood, urine and throat cultures showed no pathogenic organisms. Brucella, typhoid, paratyphoid, cold and heterophil agglutinations were negative.

Chest roentgenograms taken on the fourth (figure 11) and ninth days showed

persistence of the infiltration in the left midlung and further enlargement of the hilar structures. Histoplasmin skin test was positive, but the tuberculin tests were negative.

On the ninth day, total serum protein, albumin, globulin, van den Bergh, cephalin flocculation, thymol turbidity and prothrombin were reported as normal. Influenza A (Strains PR 8 and FM 1) complement fixation tests were negative, and the influenza B was positive only on the undiluted serum.

By the eleventh hospital day the patient's temperature had slowly returned to normal. She was feeling well, and further examinations had revealed no demonstrable abnormalities. Chest roentgenogram on the fifteenth day showed resorption of the infiltration in the left lung and slight decrease in the bilateral hilar adenopathy. Blood count taken the same day was essentially unchanged. The histoplasmosis complement-fixation test was strongly positive in a dilution of 1:640. She was discharged with a diagnosis of pulmonary histoplasmosis.

The patient was readmitted on June 14, 1950 for further study, at which time she stated that she had been entirely well since her discharge from the hospital. Thorough physical examination revealed no deviation from normal. Blood count, urinalysis, serum phosphorus and serum alkaline phosphatase were within normal limits. The brucella, cold, typhoid and paratyphoid agglutinations were negative. Gastric, bone marrow and two blood cultures showed no growth of fungi. Chest roentgenogram showed complete clearing of the left lung shadow and further decrease in the bilateral hilar swelling. Repeat tuberculin tests were negative. During the six days of study she was afebrile at all times and entirely asymptomatic.

It was the conclusion that this patient had had a relatively mild form of histoplasmosis from which she had had an uneventful spontaneous recovery. The diagnosis was based upon the presence of vague, nonspecific symptoms, hilar lymphadenopathy with left pulmonary infiltration, and a very high titer in the histoplasmosis complement-fixation test, as well as the absence of other significant diagnostic data. She was seen in the clinic on three occasions during the next year and there was no evidence of any recrudescence.

Case 7. A 23 year old male pottery glaze sprayer was admitted to the University Hospital on July 23, 1951. Four weeks earlier he had noted generalized weakness, particularly in his legs. The following day he developed severe backache, aching in the thorax, and weakness accompanied by chills and fever. When his temperature on the third day reached 105° F. he was admitted to a Zanesville, Ohio, hospital. Because of diffuse pulmonary infiltration seen in the roentgenogram he was given penicillin and Terramycin. By the ninth day his temperature was normal and he returned to his work. One week before admission to the University Hospital he noted return of fever, weakness and slight cough.

Physical Examination: Temperature, 100.6° F.; pulse, 90; respirations, 21; blood pressure, 110/60 mm. of Hg. The patient was a well developed, well nourished young man appearing in good health. The only significant physical findings were an enlarged anterior cervical lymph node, a soft blowing systolic murmur heard over the mitral area, and a moderately enlarged spleen.

Laboratory Data: Blood count, hematocrit, blood sedimentation rate, urinalysis, Wassermann and Kahn tests were within normal limits. Cultures of the nose and throat showed no pathogenic organisms. Tuberculin tests were negative. Histoplasmin skin test was positive. Histoplasma collodion agglutination test taken before admission was positive in a dilution of 1:320, and another drawn on July 24 was positive in a dilution of 1:160; complement fixation test done at this time was 1:80. Fungus cultures of the blood, bone marrow and lymph node did not show growth.

Chest roentgenogram on July 24 showed bilateral symmetrical hilar lymphadenopathy, and a fine 2 to 3 mm. nodulation was seen scattered throughout all lobes (figure 12). Histopathologic examination of a lymph node removed from the right axilla on July 25 showed only mild reticulum cell hyperplasia.

During his stay in the hospital his temperature reached 99.6° to 100° F. each day. He felt relatively well while at rest but had considerable weakness on very mild exertion. There was only an occasional cough, not productive of sputum.

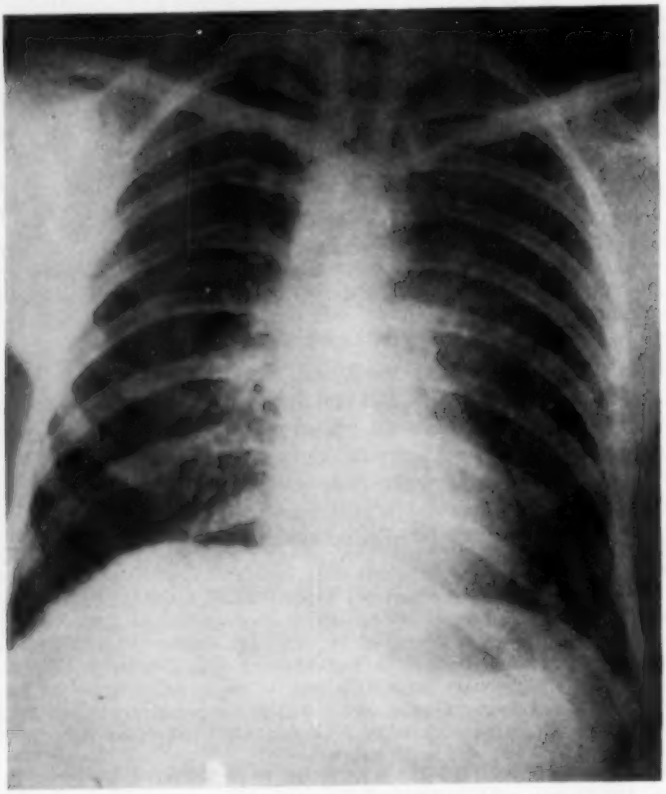


FIG. 12. *Case 7.* Chest roentgenogram taken on July 24, 1951, shows bilateral hilar lymphadenopathy and fine diffuse nodulation throughout both lungs.

Although it was not possible to isolate the organism, a diagnosis of histoplasmosis was made on the basis of the serologic studies and the clinical manifestations. He was discharged after four days to be followed by his family physician.

The patient was uncoöperative and would not return to the hospital for further study. However, it is known that he continued to have recurrent bouts of fever, cough and moderate dyspnea, along with the persistence of the disseminated pulmonary lesions for several months. No further follow-up has been possible. However, it was of interest that his brother, who was admitted a year later to the Ohio

Tuberculosis Hospital with a similar illness, was proved to have histoplasmosis by both culture and serologic tests.

Spontaneous Canine Histoplasmosis

Since central Ohio is an area with high incidence of histoplasmin reactors and pulmonary calcifications in man, it was postulated that perhaps some of the calcifications seen in the lungs of dogs living in this area also might be the result of infection with *H. capsulatum*. Little was known previously about canine histoplasmosis, since only 12 cases had been reported through 1948.[10]

Up to the present time more than 5,370 dogs admitted to the Ohio State University Veterinary Clinic have been tested with histoplasmin. Of the

Table I

A Summary of Clinical Signs and Laboratory Findings in 62 Cases of Canine Histoplasmosis

Signs	No. of Dogs*
Pulmonary nodules on x-ray	36
Dysentery	26
Cough	24
Irregular leukocytosis	22
Enlarged lymph nodes other than mesenteric	22
Anorexia	21
Enlarged, palpable mesenteric nodes	20
Emaciation	18
Vomiting	17
Dermatitis	15
Irregular fever	13
Dyspnea	9
Anemia	8
Asymptomatic	6
Arthropathy, lameness	6
Enlarged liver	5
Enlarged spleen	4
Ascites	4
Icterus	3

* Fifty-four of the 62 dogs in this series were tested with histoplasmin and all were positive except 1.

102 reacting, 62 were shown to have active histoplasmosis by culture and/or biopsy. Therefore, in contrast to the skin test in humans, a histoplasmin skin reaction in dogs often indicates active disease.

Although it is not in the province of this paper to discuss canine histoplasmosis in detail, the symptomatology and pathology of the disease in the dog have a remarkable similarity to the disease in man. Table 1 lists the predominant features of histoplasmosis in the dog.[11]

It will be seen from the above table that the most common lesions are found in the pulmonary and gastrointestinal tracts. As in man, histoplasmosis in dogs has varied greatly in severity, ranging from a benign asymptomatic form to very fulminating, disseminated disease. In five dogs we have demonstrated *H. capsulatum* by culture and/or histologically in biopsies of pulmonary lesions that ultimately went on to calcifications.[12]

This observation greatly strengthens the hypothesis of the relationship of *H. capsulatum* infections to pulmonary calcific lesions in man.

Experimental Canine Histoplasmosis

A handicap in the study of histoplasmosis has been the lack of a large animal in which histoplasmosis can be established with regularity to study the pathogenesis as well as the effect of chemotherapeutic agents. We have been impressed with the relative difficulty in establishing active disease in both dogs and mice. In mice it was necessary to employ mucin as an adjuvant to induce infection regularly.[13] Similarly, when using the mycelial phase we were unable to establish disease when introducing large inocula by intratracheal, intravenous, intramuscular and gastrointestinal routes. However, we have recently been able to establish disease regularly by the intratracheal injection of the yeast-phase organisms, and of the mycelial phase when accompanied by administration of cortisone.[14] The introduction of yeast-phase organisms into dogs by other routes did not cause clinical disease. The difficulty of establishing clinical histoplasmosis in these animals, even with massive doses, suggests that most animals, and probably man under ordinary circumstances, are quite resistant to infection with *H. capsulatum* and rarely develop clinically recognizable illness. These organisms, like other fungi, are "opportunists," and the many possible factors which permit their invasion and favor their propagation and dissemination are not known.

Diagnostic Methods

Once the suspicion of histoplasmosis has been aroused, the proper utilization of the available diagnostic methods is essential.

Skin Test: It should be emphasized that a histoplasmin skin reaction means no more than does a positive tuberculin test. It indicates *only* that the patient has been infected with *H. capsulatum*, or other antigenically related agents, at one time or another. It is *not diagnostic* of existing active infection. In a young child or in a person who has recently converted from negative to positive, it is of greater significance. A negative skin test may rule out active histoplasmosis, although more than half of severely ill patients may not react.

Repeated skin testing with histoplasmin, once a reaction has been elicited, is to be condemned. No added information can be obtained from this practice, and we have recently demonstrated that false-positive serologic reactions may result after more than one positive skin test. In our experience, after two or three weakly positive intradermal tests, "normal" individuals may develop transient serologic titers compatible with active histoplasmosis.[15, 16] A single positive skin test or repeated negative tests did not influence the serologic reaction. We have shown that repeated skin tests with histo-

plasmin did not result in enhancement or depression of the skin reactivity, nor did it result in conversion or reversion.[15]

Serologic Tests: A presumptive diagnosis can usually be established by serologic methods. In fact, a significant serologic reaction has often led to a successful search for *H. capsulatum*.[7] In our studies, the histoplasma collodion agglutination and the yeast-phase complement fixation tests have been employed.[17, 18, 19] The former becomes positive in the first two or three weeks of the disease and may become negative as early as the third or fourth month. The transient nature of this antibody response is somewhat analogous to that observed with the precipitin test for histoplasmosis,[20] except that in the latter procedure the duration of antibody titer is even shorter. Occasionally in fulminating disease a negative collodion agglutination test may be observed. The collodion agglutination test is of value because of (a) its relative simplicity; (b) stability of antigen, and (c) its not being affected by anticomplementary serum.[21]

Reactions in the complement-fixation test employing yeast-phase antigen will frequently become positive as early as the third or fourth week of the disease, and may become negative as early as the fifth to eighth months. It may "plateau" and remain positive in low dilution for as long as 12 to 18 months. Thus, in these latter periods it may be difficult to determine whether a low titer represents disease, convalescence, or nonspecific reaction. As with collodion agglutination, negative results may be obtained in fulminating disease.

The complement fixation test employing histoplasmin as the antigen has been of value in the diagnosis of histoplasmosis.[22] However, repeated positive skin tests may result in positive serologic reactions in normal volunteers with all three tests, but the titers remain positive for much longer periods (eight to 10 months) with histoplasmin complement fixation than with yeast-phase complement fixation or collodion agglutination tests (20 weeks).[16] Thus, one must be even more cautious in evaluating serologic data with this antigen when more than one positive skin test has been applied.

Culture: Once histoplasmosis is suspected based on the clinical picture and/or the serologic reaction, an intensive search should be made for the causative fungus. Although *H. capsulatum* may be recovered on the initial attempt, several cultures should be made. In our experience the best results have been obtained from blood, bone marrow and biopsy material. The organisms have been recovered from bronchial aspirate, gastric washings and scrapings from ulcers. In our laboratory relatively large amounts of the test material are inoculated directly on a 1 per cent dextrose-veal or brain-heart infusion agar (pH 7.2–7.4), containing penicillin and streptomycin to inhibit bacterial contaminants. Neither penicillin nor streptomycin depresses the growth of *H. capsulatum;* in fact, it has been demonstrated that streptomycin enhances the in vitro growth of the fungus.[23] The culture plates are incubated at both room temperature and 37° C. Although

growth may be seen as early as the tenth day, the cultures should not be discarded as negative until at least eight weeks.

Biopsy: Histopathologic study of lymph nodes, mucocutaneous ulcers, and pulmonary and bronchial tissue removed at bronchoscopy may be of value in establishing a diagnosis. It is important when culturing biopsy tissue to grind the specimen thoroughly so that a thick suspension can be inoculated directly on the culture media. In view of the fact that this fungus is an intracellular parasite, failure to take this precaution may contribute to the inability to grow the fungus.

Epidemiology

Although extensive investigations have been conducted during recent years, relatively little is known of the epidemiology of histoplasmosis. A wide variety of factors are being investigated, such as animals, soil, humidity, wind currents, water and crops. Epidemics have been described from such varied sources as pigeon excreta in a water tower, a silo, a cave, chicken houses, a storm cellar and an owl's nest.

To date, histoplasmosis has been observed in dogs, cats, rats, mice, skunks, cattle, horse and kodiak bear. At this time it is difficult to determine whether these animals may serve as a reservoir for the disease in man or whether they become infected from the same source as do humans. Since the spores of fungi, including those of *H. capsulatum,* are considerably lighter than grains of pollen, it is conceivable that air-borne infections with these agents may readily affect both man and animals in endemic areas.

Based on studies in the dog, we have demonstrated that there are at least four potential routes of dissemination of *H. capsulatum:* (1) sputum; (2) urine; (3) feces, and (4) saliva and vomitus.[24] The importance of ectoparasites in the spread of the fungus is not known. A study of 68 humans with prolonged household contact with 11 dogs clinically ill with histoplasmosis has not elicited any evidence of spread from the infected animals to man.[24] Although laboratory infections have been reported by others, 42 laboratory workers and animal attendants who have participated in our studies of histoplasmosis over a five year span, with exposures varying from three months to five years, have shown no evidence of active histoplasmosis.

Therapy

At present there is no satisfactory specific therapeutic agent. The evaluation of any medication for treatment of histoplasmosis will always be difficult because of the marked variation in the clinical course of the disease and the relative scarcity of patients for study. Ethyl vanillate has shown some promise in the treatment of active histoplasmosis, but its relative toxicity and difficulty of administration are deterrents to its widespread use.[25] Atabrine, because of its high concentration in reticuloendothelial tissues, has

been investigated by our group as a fungistatic agent, and has been found to inhibit growth of *H. capsulatum* in the test tube and to increase the survival rate of mice experimentally infected with the fungus when therapy was started early.[26] If therapy was delayed until the animal was extremely ill, no benefit was observed. It is too early to evaluate the effect in humans. However, in two fatal cases with extensive dissemination, we were never able to recover the fungus, ante mortem or post mortem, once Atabrine therapy was started.

All of the sulfonamides and the antibiotics in current use have proved ineffective in the treatment of active histoplasmosis. In fact, we have shown that streptomycin enhances the in vitro growth of *H. capsulatum*,[28] and it has been our clinical impression that in both man and dog the administration of streptomycin may have aggravated the symptoms, although this phenomenon was not observed in mice.[27]

Thus, present treatment of histoplasmosis is still largely supportive, in a manner similar to the long established therapy for tuberculosis.

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ROLE OF THE FRIEDLÄNDER BACILLUS IN CHRONIC RESPIRATORY DISEASE *

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THE Friedländer bacillus, pneumobacillus, *Bacillus mucosus capsulatus*, or *Klebsiella pneumoniae*, is usually considered to be an uncommon cause of pneumonia, a rare cause of meningitis or primary peritonitis, and an occasional urinary tract pathogen, but it is seldom mentioned relative to benign chronic respiratory disease. Yet this pathogen seems to have unique properties which make it unusually well able to persist as a low grade, chronic invader of structurally normal bronchi, sinuses and urinary tract. The type of pneumonia usually produced by this infection is exceedingly fulminating, with a marked tendency to produce lung cavitation, and it carries a high natural mortality rate variously reported as 30 to 50 per cent. With a few exceptions, these infections are resistant to penicillin and the sulfonamides, and their early recognition is demanded if cure by the use of the newer broad spectrum antibiotics is expected. From the cases presented below, it is considered likely that many milder Friedländer pneumonias go unrecognized or, because of their failure to respond to routine therapy, are termed "virus" pneumonias and end as chronic Friedländer bronchitis, chronic lung abscess or bronchiectasis.

Presented below are eight cases encountered in a period of two years, demonstrating the relative ubiquity of this pathogen and its importance in relatively benign chronic disease.

CASE REPORTS

Chronic Bronchitis:

Case 1. This 19 year old white female had had pneumonia with high fever and delirium lasting less than two weeks in 1949, four years before admission. Since that time she had had a chronic cough productive of as much as one cupful of yellowish sputum daily. In spite of this her general health was good and she had twice become pregnant. Routine chest x-ray showed some increase in vascular markings throughout the lung. Bronchograms were normal. Initial sputum culture was reported to show mixed streptococci, gram-negative diplococci, and staphylococci. Treatment for two weeks with Aureomycin and streptomycin did not alter the character or amount of the sputum. Re-culture of the sputum by means of heavy inoculum streaking of fresh sputum on a blood agar plate in the presence of antibiotic blotter tablets revealed a heavy growth of typical Friedländer colonies adjacent to the bacitracin tablet. When the organism was fished from this plate and retested against available antibiotics, its growth was found to be slightly inhibited by chloramphenicol and Terramycin but to be unaffected by Aureomycin, streptomycin and polymyxin, and to be augmented in growth by penicillin and bacitracin. Administration of chloramphenicol in a total dosage of 14 gm. was ineffective. A combined course of oral chloramphenicol

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col, Terramycin aerosol, oral sulfamerazine and trysin aerosol resulted in cure of the infection. There continues to be a slight unproductive cough, four months after completion of therapy.

Case 2. A 56 year old white male had had a chronic productive cough for 12 years; the cough had become worse in 1943 after development of pneumonia, and had left empyema requiring rib resection and drainage. X-rays at the present time showed bilateral maxillary sinusitis and pleural scarring at the left base. Bronchograms were normal. Initial culture of 24 hour sputum specimens showed *Neisseria catarrhalis* and streptococci. Treatment with penicillin and streptomycin resulted in change in color of the sputum from a thick, yellowish material to glairy, greenish sputum which, on re-culture, showed the presence of Friedländer bacilli. These were sensitive to chloramphenicol and Terramycin. Administration of chloramphenicol resulted in complete cure. The patient has remained free of chest symptoms for three years.

Case 3. This 40 year old white female had had a cough for two months which had not responded to medication with penicillin and antihistamines. The cough was almost unproductive, and the patient had had no fever but had had recurrent episodes of general body aching. Chest x-ray was normal. Culture from the sputum revealed a heavy growth of Friedländer bacilli sensitive to Terramycin, Aureomycin and streptomycin. A 10 day course of Aureomycin resulted in complete clearing of the sputum. In two months time the patient had gained eight pounds in weight, which was attributed to her unusual feeling of well-being.

Asthma with Bronchitis:

Case 4. A 52 year old white female had had perennial vasomotor rhinitis for 15 years and chronic low-grade asthma for three years, with moderate paroxysmal asthma for one month. She had raised some purulent sputum in midmorning for several years. Chest x-rays and bronchograms were normal. Bilateral maxillary sinusitis was demonstrated by x-ray. Friedländer bacillus was cultured from the sputum and reported sensitive to streptomycin. Intramuscular streptomycin followed by a five day course of chloramphenicol resulted in complete clearing of the sputum. The patient has remained free of asthma for the past two years, though watery rhinorrhea is frequently present.

Case 5. A 44 year old white male gave a history of chronic cough and rhinitis since his 'teens. Perennial asthma had begun in 1945, and was characterized by the continuous raising of yellowish sputum. He had received penicillin and sulfonamides on several occasions for colds, but such treatment had never succeeded in freeing the sputum of pus. He was first examined in 1952, after an unusually severe series of attacks, at which time severe pulmonary emphysema, polycythemia and cough productive of large amounts of gray-green, glairy sputum were evident. Chest x-ray was clear except for the emphysema. Frontal and maxillary sinuses were densely clouded. Culture of the sputum was positive for Friedländer bacilli. The sputum cleared readily on combined chloramphenicol and streptomycin therapy. Since that time the patient's asthma has been relatively mild and the sputum has remained free of pus. Cor pulmonale incident to the emphysema has been the main therapeutic problem.

Case 6. A 67 year old white female had had asthma and productive cough for 15 years. The sputum had been yellowish as long as she could remember. Culture of the sputum revealed mixed streptococci, staphylococci and Friedländer bacillus. The latter was sensitive to streptomycin and Terramycin. Administration of both drugs for a period of two weeks resulted in complete clearing of the sputum. Although ACTH or cortisone had been required to control asthma, this has not been necessary recently.

Bronchiectasis:

Case 7. A 35 year old white male had a history of pneumonia "six or seven times" as a child. Diagnosis of bronchiectasis of the left upper lobe was made in 1939, and lobectomy was advised but refused. New bronchograms showed some bronchiectasis of the right middle and lower lobes, and of the left lower lobe and lingula of the left upper lobe. The left ethmoid cells and both maxillary antra were clouded. Culture of the sputum at this time showed a heavy growth of pneumococci. Administration of procaine penicillin in a dosage of 600,000 units daily for six days resulted in change in appearance of the sputum from a yellowish, cheesy material to greenish sputum of equal quantity associated with increased malaise and cough. Re-culture of fresh sputum at this time showed Friedländer bacilli sensitive to chloramphenicol and Terramycin. Administration of chloramphenicol resulted in change of the sputum to its previous character. It was judged unwise to attempt further antibiotic treatment, as it was felt that his mixed bacterial flora had been in the most satisfactory equilibrium before treatment.

Lung Abscess:

Case 8. A 36 year old white male had had a chronic postnasal discharge and general malaise for six months prior to the development of an acute pulmonary infection with chills and fever to 104° F. Recovery on penicillin treatment had been slow, and after one month a rounded mass was demonstrated in the right lower lobe. Shortly before his first examination the patient had coughed up a large amount of greenish sputum. X-ray of the chest on admission showed an abscess cavity in the right lower lobe. Bronchoscopy demonstrated no tumor, and the sputum was negative for malignant cells. Sinus x-rays were negative. Sputum culture showed Friedländer bacilli. Administration of streptomycin and chloramphenicol resulted in closure of the abscess cavity in one week and cessation of postnasal discharge. He has remained entirely well for a period of eight months.

Discussion

The importance of chronic bronchial obstruction and infection in the pathogenesis of emphysema and bronchiectasis has been well detailed.[1, 2, 3] This urges the necessity for search for an obscure Friedländer infection in every case of chronic bronchitis and sinusitis which has not responded to the usual measures and in which infection is frankly evident from the character of the sputum. In the authors' cases, the history of previous unsuccessful penicillin therapy and of the raising of a peculiarly green, putrefactive sputum was often the lead which directed a persistent search for Friedländer bacillus. In several instances, change in appearance of the sputum from yellowish to green while the patient was on antibiotic treatment resulted in a re-check of the sputum culture and the demonstration of previously overlooked Friedländer bacillus.

The Friedländer bacillus is often confused culturally with *Aerobacter aerogenes,* which it closely resembles. Kaufman [5] doubts that a distinction exists, and has suggested that the species Aerobacter be discontinued and included with the Klebsiella. It is the custom in many laboratories to report cultures on the basis of source,[4] terming them Aerobacter when obtained from urine or abdominal infections, and Klebsiella when obtained from

sputum. The authors can well recall an unfortunate case in which a growth of *A. aerogenes* from the sputum of a lung abscess was dismissed as a trivial contaminant. The morphologic similarity of this organism to the ubiquitous *B. coli* has misled many bacteriologic technicians to dismiss it from pathogenetic consideration in the evaluation of the sputum pathogens, while they faithfully report streptococci and staphylococci, which may be no more than innocent bystanders, as in the cases cited above.

In the isolation of this pathogen we have found the best method to be the blotter antibiotic inhibition of a blood agar streak taken direct from a single fresh bolus of sputum. This often enables the technician to recover the Friedländer bacillus from the mixture of other bacteria by reason of its different spectrum of inhibition and its typical large, gray-white, very mucoid growth. It may also be discovered after planting of sputum on Sabouraud's medium, where it is one of the few bacteria which grow well.

The need for specific testing of the antibiotic sensitivity of the recovered organism in each case should be evident from the observations above, in which on three occasions the organisms were resistant to streptomycin, on three occasions to chloramphenicol, and on two occasions to Terramycin or Aureomycin. In all of these cases complete resistance to penicillin was characteristic. The most consistently effective drug was chloramphenicol, a drug whose dangers might preclude its use without specific indication of its indispensability.

The marked clinical improvement which resulted in the three cited cases of bronchial asthma suggests that in this disease, where the elimination of all bronchial infection is so necessary for improvement in the clinical status, the Friedländer bacillus should be particularly sought.

Summary

The cases cited illustrate the common occurrence of the chronic Friedländer infection as a factor in chronic sinusitis, chronic bronchitis, bronchial asthma, bronchiectasis and lung abscess. It is shown that the clinical methods necessary for its demonstration are simple, and depend for their success mostly on the interest of the clinician and laboratory in the search. Treatment was satisfactory in seven of eight instances. The single failure was in a case of bronchiectasis.

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MUSHROOM POISONING: A REVIEW OF THE LITERATURE AND REPORT OF TWO CASES CAUSED BY A PREVIOUSLY UNDESCRIBED SPECIES*

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LITTLE information is available in the British and American literature on mushroom poisoning. Smith [1] described a wide variety of poisonous and allegedly poisonous mushrooms in a recent text. Cases of poisoning recorded in the medical literature are invariably attributed to the amanita group, the *Amanita phalloides* and the *A. muscaria* being the usual culprits. We recently had an opportunity to observe and treat two cases of unquestionable mushroom poisoning, caused by a hitherto undescribed poisonous species. One of the patients was critically ill, demonstrated many of the features which fit the classic description of *A. phalloides* poisoning, and developed a complete adynamic ileus, previously unreported in this type of illness.

There is an extensive literature on mushroom poisoning in addition to what little is available in the English language. Indeed, a survey of this literature takes one on a worldwide tour, with reports from distant parts of the globe, including Australia,[2, 3] Japan,[4] the Philippines,[5] India,[6] Africa [7] and South America,[8, 9] as well as numerous reports from all parts of the European continent. There is no doubt that the disease was well recognized in many earlier civilizations. The earliest recorded cases of poisoning are attributed to the Greek poet, Euripides, whose wife together with three children died as a result of eating poisonous mushrooms (Fifth Century B.C.). Mushroom poisoning has been and is a serious problem on the European continent. Ford [10] reviewed the French literature in 1923 and collected 990 cases of mushroom poisoning, of which 381 were fatal. On the other hand, poisoning seemed to be rather rare in Great Britain. Birch [11] stated that the Registrar General's records revealed 38 fatal cases of fungus poisoning in England and Wales between 1920 and 1945. Dubash and Teare [12] were able to collect 21 cases of presumable *A. phalloides* poisoning from the London daily press over a 15 year period ending in 1945. The implication was that these authors were able to find few reports in the British medical literature during that period, which our survey confirmed. The American medical literature also contains few articles on the subject since the report of Vander Veer and Farley [13–21] in 1935.

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Ford [22] contributed a great deal to our understanding of mushroom poisoning, or mycetismus, and classified cases into five groups on the basis of predominant symptomatology:

1. Mycetismus gastrointestinalis, a mild illness with nausea, vomiting, diarrhea and a rapid recovery.
2. Mycetismus choleriformis, a more severe gastroenteritis, followed by evidences of severe liver and kidney damage and terminal central nervous system symptoms. This group is usually caused by the varieties of *A. phalloides*, and the mortality rate is quoted as from 50 to 90 per cent.
3. Mycetismus nervosus, with an initial gastroenteritis, followed rapidly by salivation, perspiration, lacrimation, confusion, delirium, convulsions and coma. This type is produced by mushrooms which contain muscarine, and *A. muscaria* and *A. pantherina* are the most common offenders. Death occasionally occurs, but the symptoms usually respond quite readily to atropine.
4. Mycetismus sanguinareus, with an initial gastroenteritis, followed by hemolysis, jaundice and hemoglobinuria. The mushroom *Helvella (gyromitra) esculenta* is responsible for this picture.
5. Mycetismus cerebralis, with transient excitement and hallucinations.

Of these groups, type 1 may occur often and not be recognized as mushroom poisoning. Types 2 and 3 have been encountered in this country, whereas types 4 and 5 are apparently uncommon.

The fatalities are almost invariably produced by or attributed to *A. phalloides*. Vander Veer and Farley reported in detail upon postmortem findings in several such cases. The important clinical features of *A. phalloides*

TABLE I

Mushroom Poisoning

	Rapid Type	Delayed Type
Causative Agent	*Amanita muscaria* group	*Amanita phalloides* group
Onset of Symptoms	From within a few minutes to three hours after ingestion.	From six to 15 hours after ingestion.
Symptoms	Excessive salivation and lacrimation; pupils contracted and not reacting to light or to accommodation; nausea and vomiting; abdominal pains with profuse watery evacuations; pulse at times slow and often irregular; dizziness and confusion with convulsions and coma in severe cases; fatal cases, death within a few hours.	No symptoms for several hours; onset sudden with severe abdominal pains; nausea, vomiting, and usually diarrhea; vomitus and stools often showing blood and mucus; extreme thirst; anuria at times, usually jaundice in from two to three days; cyanosis and coldness of the extremities; increasing prostration with coma and death; fatal cases, death usually from fifth to eighth day.
Prognosis	Good in mild cases; good in severe cases if patient is treated with atropine.	Grave; mortality, from 50 to 70 per cent, often 100 per cent of a group.

and *A. muscaria* poisoning are presented in table 1 (from Vander Veer and Farley [21]).

Marcovitz and Alpers [22] reviewed the literature with respect to neurologic findings and provided a detailed description of the neuropathologic lesions in two fatal cases. Clinically, almost every neurologic manifestation has been described. In a given patient symptoms may include any of the following: convulsions, delirium, exaggerated deep tendon reflexes, positive Babinski reflexes, oculomotor and pupillary changes, hypotonia, areflexia, incontinence, somnolence, opisthotonos, catatonic reactions, sensory disturbances, paralysis of the bladder and sphincter spasm, and weakness and paralysis of the extremities. Kulik [24] recently described acute psychoses. The central nervous system manifestations were first considered secondary to either the renal or the hepatic injury. However, Marcovitz and Alpers demonstrated widespread damage to the brain, including edema, congestion, scattered punctate hemorrhages, cortical areas of erosion, perivascular infiltration, and fatty infiltration in the ganglion cells, neuroglia, microglia, ependyma and endothelium.

Two cases recently encountered are reported herewith, one of which developed severe gastrointestinal, genitourinary, hepatic, cardiovascular and central nervous system injury, with recovery.

Case Reports

Case 1. A 40 year old male picked some mushrooms from a neighboring lawn and ate about one and a half cupfuls fried with scrambled eggs on January 21, 1953, at 6:00 p.m. He was perfectly well until he awakened at 4:00 a.m. the next morning with violent nausea and vomiting, followed soon after by watery diarrhea. He was hospitalized at 7:00 a.m.

Past history was entirely negative except that a borderline hypertension, 140/94 mm. of Hg, had been observed on several occasions.

Physical examination revealed the patient to be acutely ill, with a temperature of 101° F., a blood pressure of 98/60 mm. of Hg, and a heart rate of 90 per minute. Otherwise there were no specific abnormal findings. Laboratory findings were all normal except for the urine, which showed 1 plus albumin and occasional finely and coarsely granular casts.

The patient was permitted nothing by mouth, was given salt, water and glucose by vein, and sodium phenobarbital and atropine subcutaneously, with immediate improvement. The blood pressure returned to 140/90 mm. of Hg. By the third hospital day he was able to tolerate ice by mouth without vomiting. Fever, anorexia and diarrhea persisted. On the fourth day he was able to eat Jello and ice-cream for lunch, but by evening of that day he rapidly became distended and developed the picture of a complete paralytic ileus (figure 1). Vomiting recurred, producing grayish black material which gave a 4 plus guaiac reaction, as did the stools. Intubation with Levine tube failed to relieve the distention. A Miller-Abbott tube was successfully passed, a rectal tube inserted, and Prostigmin given regularly. Although the distention was gradually reduced in the next four to five days, the patient's condition deteriorated rapidly. The blood urea nitrogen rose, he became jaundiced, dullness and diminished breath sounds appeared at the right lung base posteriorly, and the blood pressure rose to 200/120 mm. of Hg. Urinalysis revealed albumin, granular casts and red blood cells. Because of the continuing fever and the pulmonary signs

he was given 500 mg. Aureomycin twice daily by vein. In spite of what was considered to be judicious use of parenteral fluids, with very little sodium, the patient developed 3 to 4 plus dependent subcutaneous edema and a thrombophlebitis of both arms with 3 to 4 plus edema (possibly related to the intravenous Aureomycin). On the eleventh hospital day the patient had a generalized convulsion, became comatose, and continued to deteriorate. Figure 2 presents a summary of the important labora-

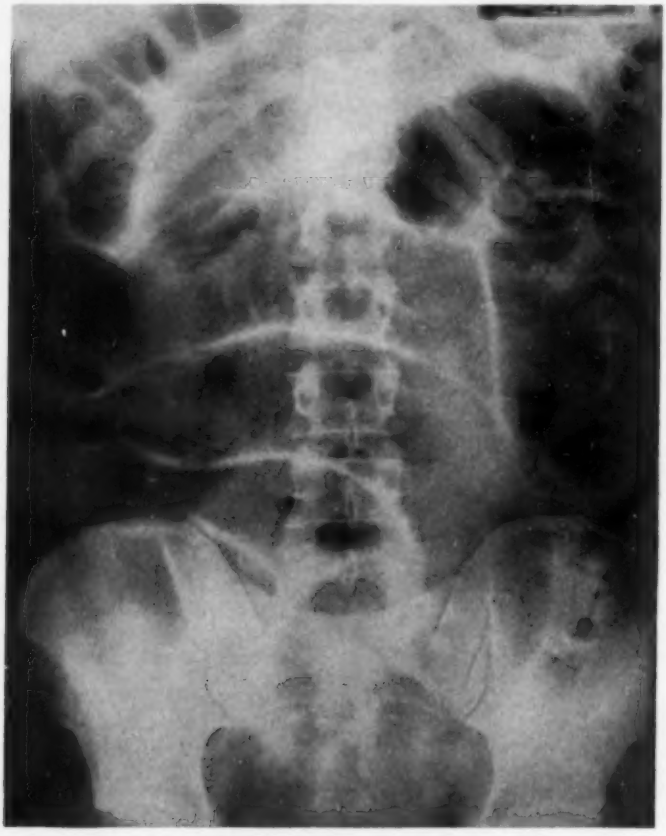


FIG. 1. Anteroposterior film of abdomen (supine).

tory and clinical findings. The blood urea nitrogen gradually rose in spite of good urine volumes, reached a peak of 145 mg. per cent on the thirteenth hospital day, and then gradually fell. Icterus was first apparent on the second day. The total bilirubin (van den Bergh) reached a peak of 12.1 mg. per cent on the tenth day, then gradually fell. Cephalin flocculation test was 4 plus. The prothrombin time was 30 per cent of normal on the seventh day. This improved with parenteral administration of vitamin K. On the fourteenth and fifteenth hospital days the patient was given salt-poor albumin intravenously. On the fourteenth day in addition to his coma he

demonstrated opisthotonos, nuchal rigidity and bilateral Kernig's and Brudzinski's reactions. Lumbar puncture revealed xanthochromia, a pressure of 300 mm. H_2O, a protein of 180 mg. per cent, and the presence of 100 crenated red cells per cubic millimeter (figure 2). On the fifteenth day, immediately after an albumin infusion, he developed acute pulmonary edema with many medium and coarse moist râles, a

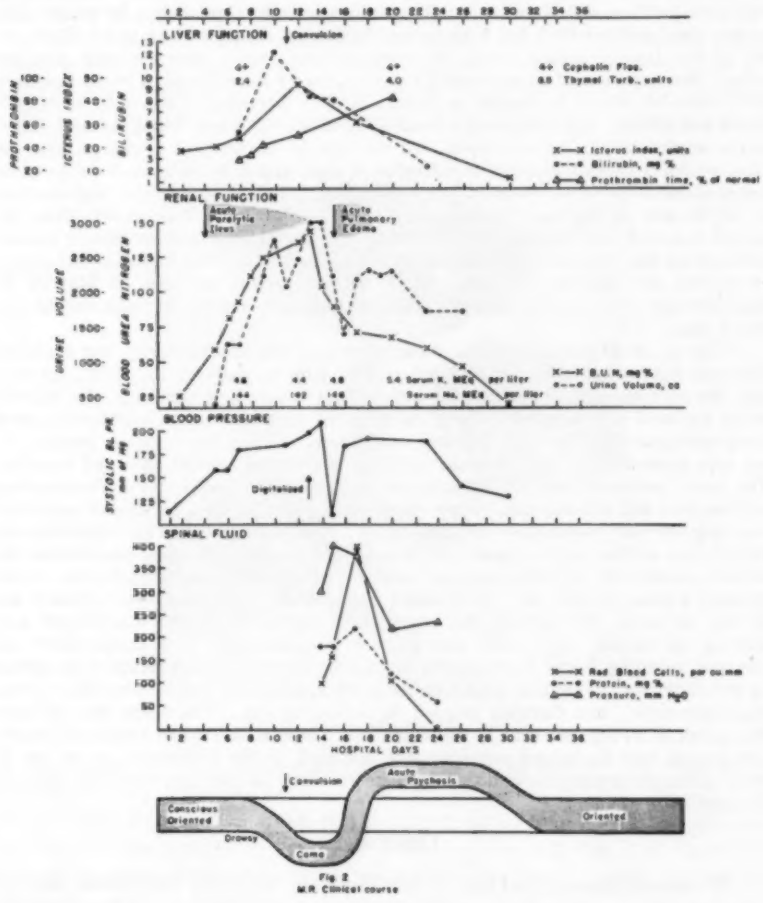


Fig. 2
M.R. Clinical course

FIG. 2.

gallop rhythm, and pink frothy sputum which had to be aspirated via nasal catheter. The patient had been given intravenous digitoxin two days earlier, and at this point was placed in an oxygen tent and tourniquets were applied to all extremities. He appeared moribund, with Cheyne-Stokes respirations. The blood pressure, which had fallen from its previous hypertensive level to 110/70 mm. of Hg, returned to 210/120 mm. of Hg. Serial electrocardiograms exhibited a flattening of T waves in

Leads I and II and an inversion of T waves in V_{3-6}, without ST segment changes. The pulmonary edema gradually disappeared, and the diuresis which had begun five days prior continued. There was some apparent response by the seventeenth day, but the signs of meningeal irritation persisted, and the spinal fluid revealed somewhat greater protein and many more cells. The patient gradually recovered consciousness but was now completely disoriented, with hallucinations and delusions. This clinical state continued, as did his fever, until the thirty-second hospital day, by which time he was clear and oriented, but with no recollection of events leading to his illness or any of the days preceding coma. Memory of these events later returned, and the patient then experienced an uneventful recovery, except for a stubborn *proteus* urinary tract infection, which responded to Gantrisin after Terramycin and dihydrostreptomycin had failed. He was given a total of 1,500 c.c. of whole blood because of the severe anemia which had developed. At the time of his hospital discharge, after 46 days, cephalin flocculation test remained at 4 plus, and bromsulfalein liver function test revealed 14 per cent retention in one-half hour. His blood pressure had returned to 140/90 mm. of Hg, and the urine was essentially normal. Two months later the patient was still convalescing, demonstrating easy fatigability and occasional nausea, although he had regained 20 of the 40 pounds he had lost. The cephalin flocculation test at this time was again 4 plus. When the patient was last seen, on May 21, he was clinically better, he had regained his normal weight, and the cephalin flocculation was 1 plus.

Case 2. A 40 year old female (wife of case 1) ate approximately one cupful of the same mushrooms with her husband at 6:00 p.m. on January 21, 1953. At 4:00 a.m. the next morning she awakened with violent nausea and vomiting. In contrast to her husband, who vomited nothing but bile, this patient's vomitus contained a great many undigested and partially digested mushrooms. When first seen, on January 22, she was moderately ill with nausea, vomiting, crampy abdominal pain and diarrhea. The blood pressure was 130/80 mm. of Hg. Subcutaneous sodium phenobarbital and atropine did not alleviate her symptoms to any degree, and because of continued vomiting she was hospitalized on January 23. Her blood pressure on admission was 114/70 mm. of Hg, and her heart rate was 96 per minute. Physical examination revealed a moderately ill woman with no positive findings other than dehydration. Urine revealed a trace of albumin. Blood count was normal. The blood urea nitrogen was 25 mg. per cent. Her course was essentially a benign one. She was treated with nothing by mouth, salt, water and glucose intravenously. The temperature was elevated, reaching 101.6° F. orally on the third hospital day and returned to normal by the sixth day. Vomiting ceased on the sixth hospital day (seven days after eating the mushrooms), and diarrhea stopped the following day. The blood urea nitrogen had fallen to 16 mg. per cent by the third day. Icterus index had remained normal. The patient was discharged, asymptomatic and well, on the fourteenth day of her illness, although bromsulfalein determinations revealed 12 per cent retention after 30 minutes.

Discussion

It was anticipated that case 2 would not be seriously ill because she had vomited up a considerable amount of mushrooms. In case 1 (the husband) we did not know what to expect; the literature dealt primarily with *A. phalloides* poisoning, which we were certain this was not, first, because the mushroom had been identified as a definitely different species, and second, because *A. phalloides* has never been found in Oregon. The fact that the course followed the classic description of *A. phalloides* poisoning, from the 10-hour

latent period to the disastrous effects upon the organ systems involved, suggests that the mushroom eaten contained the same or a similar poison. There are statements in the literature that if a case of mushroom poisoning exhibited these features, i.e., a 10 to 12 hour latent period and severe damage to the liver, kidneys and brain, it was definitely the result of *A. phalloides.*[11, 25] Obviously this can no longer be considered a valid hypothesis.

The mushroom in question was identified by Dr. A. H. Smith, of the Department of Botany of the University of Michigan, as a previously unidentified specimen of the genus Galerina.* Unfortunately, fresh specimens were no longer available for photographing, and figure 3 is a reproduction



FIG. 3. *Galerina venenata* Smith.

of the specimen by case 2, a professional artist. The patients had mistakenly identified the mushroom as a variant of *Amanitopsis fulva,* described in Ramsbottom's book [27] on edible fungi. Since many people pick and eat wild mushrooms, the present cases should serve as a warning that it is sometimes difficult to distinguish edible from non-edible specimens, except perhaps for the most expert mycologists.

Two other points are worthy of mention. The first is that there is no description of the spinal fluid findings in the previously described cases and in the review of neurologic symptoms by Marcovitz and Alpers. The second point is that of the complete adynamic ileus. This is unprecedented in the literature on mushroom poisoning, although the Germans did report acute

* *Galerina venenata* Smith.[26]

mechanical intestinal obstruction subsequent to eating indigestible specimens after the First World War.[28, 29] We cannot explain the ileus other than to assume that it followed the severe, necrotizing, hemorrhagic gastroenteritis or was secondary to the severe hepatic necrosis.

Treatment

Unfortunately, there is as yet no specific therapy for mushroom poisoning of the seriously intoxicating varieties. As previously mentioned, atropine is considered to be specific for the muscarine type of poisoning, but only nonspecific supportive measures are available for the more deadly *A. phalloides*. A number of years ago an *A. phalloides* antitoxin was prepared at the Pasteur Institute.[30] It is usually recommended, although there is no clear record of its effectiveness in man. It is apparently not available in this country. In 1932 Limousin and Petit,[31] noting that rabbits succumbed to the poison when injected but not when given the toxin orally, found that they could protect cats by feeding them minced raw rabbit stomach and raw rabbit brain with the poisonous mushrooms. This technic was tried on patients with what seemed at first to be success, but a subsequent report was discouraging.[32] Recently we learned that a patient in Oregon poisoned with an unknown species was successfully treated with cortisone. It is of course difficult to say now whether that illness would have been a mild one without the cortisone. We did not consider the use of cortisone in case 1 in the first three days, when the gravity of the illness had not yet become manifest. With the subsequent appearance of ileus, edema and renal failure we were very hesitant to use it. Parenteral glucose together with salt and water seem logical as the basic therapeutic measures, in spite of the failure of Wieland et al.[33] to protect mice poisoned with an *A. phalloides* toxin with glucose. In our judgment, careful fluid and electrolyte management and excellent nursing care contributed as much as any other measures to the recovery of case 1. The high mortality rate in *A. phalloides* poisoning is based on experiences 30 or more years ago. It is not unlikely that today we may be more successful because of a better understanding of salt and water metabolism and the refinements of modern intravenous therapy.

Mushroom Toxins

In spite of the frequent reports of *A. phalloides* poisoning, very little was known of the specific toxin until recently. The early work of Ford in 1906 [34] served as a classic reference for evaluating mushroom poisons. However, Ford himself admitted the difficulty of evaluating substances which were toxic for guinea pigs and rabbits on injection but were harmless to these animals when given orally. He was able to isolate a thermolabile hemolytic substance, but recognized that since most people ate this species after cooking, there was another toxin. Clark et al.[35] were able to produce

a fatal illness in a dog given *A. phalloides* per os. We fed a mongrel bitch 1.4 gm. of the dried Galerina mushrooms which the patients had eaten. This was a fairly small dose, but it did produce a mild illness with vomiting and diarrhea. In 1937 Lynen and Wieland [36] crystallized a substance from *A. phalloides* which was fatal to mice at a dose of 6.6 gamma per gram. Wieland and Witkop [37] identified this substance as a ring polypeptide and called it "phalloidin." The successful crystallization of another polypeptide called alpha amanitin was subsequently reported.[38] This material was found to have a molecular weight of 764. Since there were no free carboxyl or amino groups, and since hydrolysis yielded only amino acids, it was felt that alpha amanitin was also a ring polypeptide.[38, 39] This crystalline material was lethal for mice at a dose of 0.2 gamma per gram, producing, after a latent period of 12 to 15 hours, glycogen depletion in the liver followed by hypoglycemia, fatty degeneration of the liver, and death.[38] More recently a third crystalline toxin called beta amanitin has been isolated.[40] One can only speculate at this time as to whether these crystalline toxins are responsible for the toxic effects in man and, if so, that these cyclic polypeptides produce their generalized disastrous results by interfering with enzyme mechanisms normally utilized in protein synthesis. To suggest that certain herbivorous animals are immune because they are capable of splitting the ring structure in their digestive tracts is equally speculative.

Summary

The literature concerned with mushroom poisoning has been reviewed. The disease, while not common in Great Britain and the United States, is prevalent throughout the world and especially on the European continent.

Amanita phalloides and *Amanita muscaria* are the most common causes of poisoning. *A. phalloides* produces severe damage to the liver, kidneys and central nervous system, and is responsible for most of the fatalities.

Two cases of mushroom poisoning by a previously undescribed specimen of the genus Galerina have been reported. One of the patients suffered severe damage to the gastrointestinal, renal, cardiovascular, hepatic and central nervous systems, including a complete adynamic ileus, followed by recovery.

Acknowledgment

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ALTERED IMMUNOLOGIC REACTIONS IN SARCOIDOSIS *

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It is widely accepted that in patients with sarcoidosis tuberculin sensitivity is infrequent or is of a low level and transient in nature. The mechanism responsible for the absence or loss of tuberculin sensitivity in these patients is not known. The suggestion [1] that the low incidence of tuberculin reactions in sarcoidosis is merely the result of residence in areas of low tuberculosis morbidity is not valid, for it has been shown that patients with sarcoidosis fail to develop tuberculin sensitivity following repeated injections of BCG vaccine.[2]

The diminished sensitivity to tuberculin observed in patients with sarcoidosis has been attributed to a specific destruction of tuberculin [3] or to an action in the skin of specific tuberculin-neutralizing factors.[4] The hyposensitivity has been considered by these investigators to support the concept that sarcoidosis represents an atypical form of tuberculosis, in which anergy is associated with absence of caseation. Implicit in these theories is the assumption (for which no evidence has been presented) that the hypergy of sarcoidosis is restricted to tuberculin. To ascertain whether this abnormal behavior is limited to the tuberculin reaction, the following immunologic studies have been carried out in patients with sarcoidosis:

1. The prevalence of delayed-type skin reactions.
2. The development of delayed-type skin reactions after immunization.
3. The development of circulating antibodies after immunization.
4. Alterations of histamine and immediate type skin reactions (passive transfer studies).

Thirty-eight patients with sarcoidosis were studied. The diagnosis of sarcoidosis was made according to established criteria.[2] In every case biopsy material revealed characteristic epithelioid-cell tubercles, and special effort was made to exclude tuberculosis, beryllium poisoning and fungus infections.

Two groups of apparently healthy subjects were used as controls. The first (Group A) consisted of 71 male inmates of a prison who volunteered for the study. A second (Group B) comprised 15 subjects (10 female, five male), chiefly relatives or friends of the patients with sarcoidosis. In

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this latter group an attempt was made to secure persons with environmental and economic characteristics similar to those of the sarcoid patients. In both control groups the age and racial distribution was similar to that of the patients. Brief histories and chest x-rays were secured to exclude pulmonary and significant extrapulmonary disease.

The following antigens were used in study of delayed-type skin reactions: tuberculin, pertussis agglutinogen, mumps virus, Oidiomycin and trichophytin. Pertussis and typhoid vaccines were employed in immunization studies. Immediate type skin responses were studied by histamine wheal and flare reactions and passive transfer of ragweed pollen sensitivity.

All patients were initially tested with 0.00002 mg. PPD tuberculin. Non-reactors were retested simultaneously with 0.005 mg. PPD and 1.0 mg. O.T.[2] The pertussis agglutinogen, prepared according to the technic described by Smolens and Mudd,[5] was used in 1–10 dilution. The mumps antigen, supplied by Dr. Werner Henle, Children's Hospital, Philadelphia, Pennsylvania, was prepared from chick embryo allantoic fluid, and normal allantoic fluid was used as a control testing material. The Oidiomycin (*Candida albicans* extract) and trichophytin (*Trichophyton gypseum* extract) were used in 1–100 dilution. Skin tests were done intradermally on the volar surface of the forearm or arm, using 0.1 c.c. of antigen solution. The reactions were read within 48 to 52 hours, using the same criteria as those established for the reading of tuberculin tests.[6] Plus 1 reactions (less than 1 cm. of induration) were considered nonspecific and read as negative.

Immunization with pertussis vaccine * was accomplished by the subcutaneous injection of three doses (1.0 c.c., 2.0 c.c., 2.0 c.c.) at monthly intervals. Skin tests with pertussis agglutinogen and serum agglutinin (pertussis) titers † were done prior to immunization and at monthly intervals thereafter. The serum agglutinin titers were measured according to the technic described by Smolens and his co-workers.[7] Immunization with typhoid-paratyphoid vaccine was accomplished by the intradermal injection of three doses (0.1 c.c., 0.15 c.c. and 0.2 c.c.) at two to four week intervals. Agglutinin tests, performed prior to the first injection and four weeks following the last injection, were done according to the standard Widal technic.

Wheal and flare reactions were measured 10 minutes after the intradermal injection of 0.1 c.c. of histamine (1–100 dilution). Passive transfer of ragweed pollen sensitivity (Prausnitz-Küstner reaction) was accomplished in the following manner: 0.1 c.c. of blood serum taken from a patient with severe ragweed pollen hay fever was injected intradermally; 48 hours later, the site was challenged with ragweed pollen extract. Control intradermal skin tests with ragweed pollen extract were performed on the other forearm.

* Pertussis agglutinogen and pertussis vaccine were generously supplied by Dr. William Verwey, of Sharpe and Dohme, Inc.

† Serum agglutinin titers were performed by Dr. Joseph Smolens, of the Children's Hospital of Philadelphia.

Results

Delayed-type Skin Tests (Table 1):

1. *Tuberculin.* Thirty-eight sarcoid patients were skin-tested with tuberculin. Positive reactions were obtained in 36.8 per cent, as compared to a frequency of 66.7 per cent in control group B.
2. *Pertussis.* Application of pertussis agglutinogen to 38 sarcoid patients demonstrated reactions in 13.2 per cent, as compared to 57.0 per cent in control groups A and B.
3. *Mumps virus.* Skin reactions to mumps virus were observed in 29.6 per cent of 27 patients with sarcoidosis, as compared to 80.0 per cent in control group B.
4. *Oidiomycin.* Skin tests with Oidiomycin yielded reactions in 51.9 per cent of 27 patients with sarcoidosis, as compared to a frequency of 80.0 per cent in control group B.
5. *Trichophytin.* Reactions to trichophytin occurred in 18.5 per cent of sarcoid patients and 26.7 per cent of control group B.

Table I

Frequency of Delayed-Type Skin Reactions in Patients with Sarcoidosis

Antigen	Sarcoid					Control					χ^2
	Number Tested	Positive		Negative		Number Tested	Positive		Negative		
		No.	%	No.	%		No.	%	No.	%	
Tuberculin	38	14	36.8	24	63.2	15	10	66.7	5	33.3	3.9
Pertussis	38	5	13.2	33	86.8	86	49	57.0	37	43.0	20.6
Mumps	27	8	29.6	19	70.4	15	12	80.0	3	20.0	9.8
Oidiomycin	27	13	51.9	14	48.1	15	12	80.0	3	20.0	4.0
Trichophytin	27	5	18.5	22	81.5	15	4	26.7	11	73.3	0.38

The frequency of positive skin tests to tuberculin, mumps antigen and Oidiomycin in the control group approximates that observed in Friou's study.[8] Patients with sarcoidosis showed significantly fewer reactions to pertussis, mumps virus and Oidiomycin. Reactions to trichophytin were not significantly less frequent in this study.

Skin Test and Circulating Antibody Responses to Immunization

Twenty sarcoid patients and 10 control subjects (selected from control group "A") who were skin-test negative to pertussis agglutinogen were immunized with pertussis vaccine. Six of the sarcoid patients received two

TABLE II

Development of Skin Sensitivity to Pertussis Agglutinogen in Patients with Sarcoidosis Following Immunization

	SKIN REACTIONS	MONTHS AFTER IMMUNIZATION						TOTAL NO. OF TESTS
		1	2	3	4	5	6	
SARCOID	POSITIVE	4	2	1	1	1	1	10
	NEGATIVE	10	8	7	8	5	9	47
CONTROL	POSITIVE	4		4				8
	NEGATIVE	1		0				1

$\chi^2 = 11.8$

courses of immunization. Skin-test responses (table 2) and serum agglutinin titers (figure 1) were measured at monthly intervals. Circulating antibodies developed in normal fashion in both groups. However, only nine of the 20 sarcoid patients developed skin sensitivity, and this was in most instances temporary and disappeared after several months. Of a total of 57 skin tests done on 20 patients with sarcoidosis, 10 were positive and 47

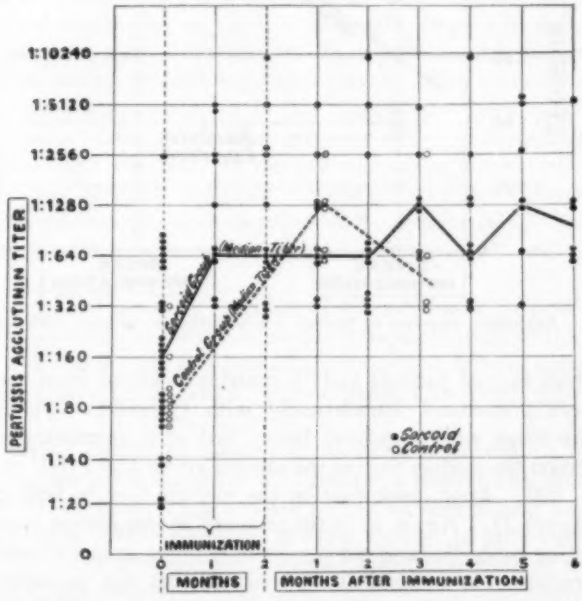


FIG. 1. Agglutinin response to pertussis immunization in patients with sarcoidosis.

were negative. Five of the 10 control subjects were retested after a course of immunization. Four were positive, and the fifth, who failed to react one month after immunization, gave a positive reaction on retest three months after immunization. The frequency of skin reactions following immunization of larger groups with the same antigen has been reported as 92 per cent in one study [9] and 100 per cent in another.[10]

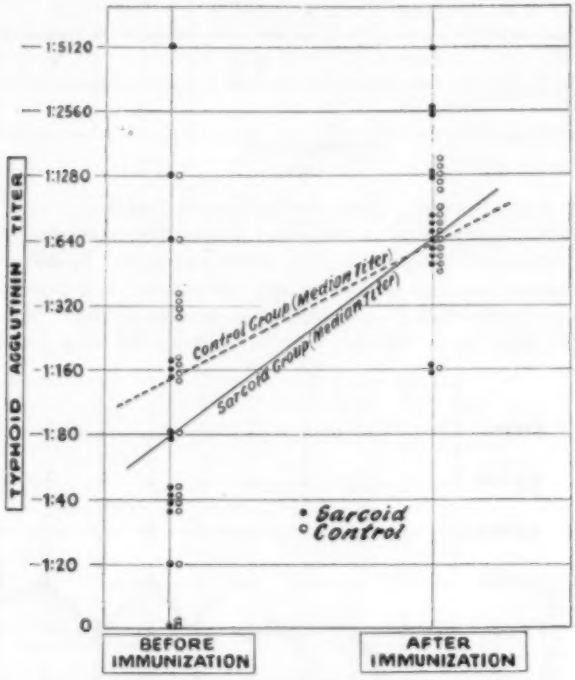


FIG. 2. Agglutinin response to typhoid immunization in patients with sarcoidosis.

Fourteen sarcoid patients and 18 controls (selected from control group "A") were immunized intradermally with typhoid-paratyphoid vaccine. Agglutinin titers were measured before and after immunization. Before immunization the median titer in the sarcoid group was 1:80; in the control group, 1:160. After immunization the median titer in both groups was 1:640 (figure 2). Again, as in the pertussis immunization study, the level of circulating antibodies was not significantly lower in sarcoid patients. The normal response to immunization indicates that the mechanism for the manufacture of circulating antibodies is intact in patients with sarcoidosis.

Histamine and Passive Transfer Studies

Twelve patients with sarcoidosis responded with a normal wheal and flare reaction when tested with intradermal injection of a 1–100 solution of histamine.

Seventeen patients with sarcoidosis were tested with ragweed pollen extract. One patient with a history of fall hay fever reacted. Passive transfer of ragweed pollen sensitivity was tested by the Prausnitz-Küstner reaction in the remaining 16 patients. Transfer of sensitivity was successfully accomplished in all cases.

These studies indicate that patients with sarcoidosis are capable of normal cutaneous responses to agents producing immediate-type reactions.

Discussion

The concept, once widely held, that sarcoidosis was an atypical form of tuberculosis rested on (1) epidemiologic, (2) pathologic, (3) bacteriologic, and (4) immunologic evidence.

1. The frequency of development of frank tuberculosis in persons with sarcoidosis, impressively high in early studies,[11] appears in recent investigations to have diminished sharply.[12] This presumably reflects the general decline in prevalence of tuberculous infection. Moreover, in the past the diagnosis of sarcoidosis often was not made until patients had been studied and even treated in tuberculosis wards or sanatoria; at present, patients with sarcoidosis are infrequently exposed to this special hazard of tuberculous infection. The recent epidemiologic observation [1] that a very large proportion of patients with sarcoidosis in this country were born in rural areas of the southeastern States is difficult to reconcile with a tuberculous etiology.

2. The histologic similarity of the granulomatous lesions which characterize these two diseases suggested a common etiology. However, the validity of this inference has been dispelled by the demonstration that similar tubercles are produced by beryllium,[13] by histoplasmosis [14] and by other infections.[15]

3. The occasional report of isolation of tubercle bacilli in persons with sarcoidosis could not be dismissed when the recognized cases of this disease were few. The number of cases adequately studied bacteriologically is now great, and the proportion in which tubercle bacilli have been demonstrated is negligible.[16]

4. The relative anergy to tuberculin observed in sarcoidosis has been interpreted by some investigators as evidence for a tuberculous etiology, on the assumption that this hypergy was due to specific neutralizing substances.

Evidence is now available to show that the hypergy of sarcoidosis is not restricted to the tuberculin reaction. Friou [8] noted that patients with sarcoidosis reacted less frequently than controls to mumps, trichophytin and

Oidiomycin skin tests, as well as to tuberculin. These observations are in accord with those of the present study on the prevalence of delayed-type skin reactions. It should be pointed out that these findings do not conclusively establish an immunologic abnormality, for it is conceivable that differences in geographic origin and residential history might be responsible for a lowered prevalence of skin sensitivity in patients with sarcoidosis. The demonstration of failure of pertussis immunization to produce a normal frequency of skin reactions in patients with sarcoidosis provides strong evidence that the immunologic defect is not restricted to the tuberculin reaction.

The relative tuberculin anergy cannot be attributed to anticutins or other neutralizing factors, since recent experiments [17] showed that on passive transfer of tuberculin sensitivity the behavior of patients with sarcoidosis was indistinguishable from controls. Inasmuch as there is no inherent cutaneous abnormality in sarcoidosis, the diminished skin sensitivity to a variety of antigens is presumably due to a failure of cellular antibodies, of the type involved in delayed reactions, to reach the skin. It remains conjectural whether the defect is in manufacture or transport of these antibodies.

The normal responses in circulating antibody titers following pertussis and typhoid immunization indicate that the impairment of immunologic mechanisms is not a general one. The defect differs from that produced in experimental animals by blockade of the reticuloendothelial system with India ink; in these studies,[18] diminution of circulating hemolysins was demonstrated.

Other diseases are responsible for impairment of immunologic reactions. It has long been known that acute exanthems such as measles may abolish tuberculin sensitivity. Impaired immunologic reactions have been described in Hodgkin's disease. De Marval [19] observed that BCG vaccination failed to produce tuberculin sensitivity in patients with this disease. It should be of interest to ascertain whether the defect in Hodgkin's disease is a general one involving circulating antibodies, as Dubin [20] has suggested, or is a limited one confined to impairment of delayed-type skin reactions, as in sarcoidosis.

Summary

1. Thirty-eight patients with sarcoidosis have been studied with a variety of skin tests and immunologic procedures.

2. Patients with sarcoidosis were found to react significantly less often than controls to tuberculin, pertussis agglutinogen, mumps virus and Oidiomycin.

3. Skin sensitivity failed to develop in normal fashion after immunization with pertussis agglutinogen, but circulating antibodies appeared in normal titers.

4. Agglutinins developed in normal titer after immunization with typhoid vaccine.

5. Normal responses were observed to passive transfer of ragweed sensitivity and to intradermal histamine injection.

6. These observations demonstrate that the immunologic defect in sarcoidosis is a limited one, apparently involving the production or transport of antibodies concerned in delayed-type skin reactions.

7. The defect is not confined to the tuberculin reaction. Hence, the relative anergy to tuberculin characteristic of sarcoidosis is nonspecific and cannot be construed as an argument for a tuberculous etiology of this disease.

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ANTIBIOTIC PREVENTION OF INTERCURRENT INFECTIONS IN DIABETES MELLITUS*

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With the steadily increasing number of elderly individuals in the general population, a greater interest in the diseases characteristic of later life has developed.[1] Outstanding among these conditions are cardiovascular disease, malignancy and diabetes mellitus. It has been estimated that almost 4,000,000 persons now living in this country will eventually have diabetes.[2] Furthermore, the outlook for the next few decades is such that the incidence of this metabolic derangement may be expected to increase twice as fast as the total population. This, of course, implies that diabetes mellitus will be an even greater medical problem in the future.

The important rôle of infection in diabetes is well established. Patients having this disease are unusually susceptible to bacterial invasion; especially is this true of the genitourinary tract, respiratory system and skin.[3] All too frequently a diabetic who has been well managed for months or even years becomes uncontrolled and rapidly acidotic as the result of an infection. At the John Gaston Hospital sudden deterioration in longstanding diabetes is usually not the result of the misuse of insulin, nor is it ordinarily caused by dietary indiscretion; rather, it probably indicates a urinary tract infection in a female or a respiratory infection in a male. It is important to realize that a minimal respiratory tract infection may be as dangerous to a diabetic as to a patient with advanced emphysema. Careful investigations have revealed that pyuria occurs five times as frequently in diabetic as in nondiabetic individuals.[4] Approximately 20 per cent of persons dying of diabetes mellitus have renal infection; acute pyelonephritis has been demonstrated to be the cause of death four and one-half times as often in diabetic patients as in controls.[5, 6] Asymptomatic pyuria and bacilluria occur frequently and may be overlooked, with resultant serious and even fatal illness.[4]

New insulin preparations, better understanding of the use of this hormone, improved concepts of nutrition, the advent of numerous chemotherapeutic agents and a vastly expanded knowledge of fluid and electrolyte principles have resulted in a striking prolongation of life in diabetics. The average age at death from 1898 through 1914 was 44.5 years, as compared with 64.5 years from 1944 through 1946.[3] Nonetheless, it must be emphasized that while this disease ranked only twenty-seventh as a cause of

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death in 1900, it had advanced to eighth position in 1943. The cause of death in diabetes is, however, quite different today from that in the past. The incidence of coma has greatly decreased. Nevertheless, this dangerous complication remains a therapeutic problem, as is well illustrated in this paper. It is important to recall that infection, along with inadequate insulin and excessive nutrition, is recognized as being one of the leading causes of this serious complication. For this reason, antibiotics are routinely employed in its treatment.[6] While the largest number of fatalities at present results from the so-called degenerative complications of diabetes, acute infection still ranks second.[5] Actually, this does not present the entire picture. It would appear that infection plays a significant rôle in the development of cardiovascular-renal side effects of diabetes. Comprehensive investigations have established that, in those cases which have been persistently well controlled, degenerative complications are encountered much later and less commonly.[7] Excellent control is of course impossible in the face of repeated episodes of infection. Recently diabetic nephropathy has been demonstrated to be the leading cause of death in young diabetic patients.[8] Histopathologic studies in this condition revealed that in most cases there is a mixed picture of acute and chronic pyelonephritis, arteriosclerosis, arteriolosclerosis and intercapillary glomerulosclerosis. Furthermore, while the exact etiology of necrotizing papillitis is unknown, it is generally accepted that infection is involved.[9] Papillary necrosis is a condition which may be unilateral or bilateral, and is a serious complication of pyelonephritis. Therefore, it is most frequently encountered in patients suffering from diabetes, urinary tract obstruction, or both.[10] It is apparent, then, that infection influences the treatment and prognosis of diabetes mellitus both directly and indirectly.

In recent years chemotherapeutic agents have been administered for prolonged periods in an effort to reduce the incidence of group A beta hemolytic streptococcal infections in rheumatic fever patients.[11] Such prophylaxis has been quite effective. It occurred to us that a similar approach to the management of intercurrent infections in diabetic individuals might also be profitable. Aureomycin has been demonstrated to be effective in the majority of common respiratory infections and is also of value in urinary tract infections.[12, 13] We had observed no serious side effects even with the prolonged administration of this antibiotic; with dosage in the range of 0.5 to 1 gm. daily, disturbing gastrointestinal symptoms were largely eliminated.[12, 14–17] Furthermore, our studies with Paraben (the methyl and propyl esters of para-hydroxybenzoic acid) had indicated that the addition of this agent to Aureomycin prevented the overgrowth of *Candida albicans*, a potentially grave problem in the treatment of diabetics.[18]

The present paper is a report of the prolonged administration of Aureomycin as a prophylactic agent to a large number of patients having diabetes mellitus. Comprehensive toxicity studies are presented.

Methods

Varying amounts of Aureomycin * were administered to a large series of patients. Subsequently, blood concentrations were determined at regular intervals. As a result of these studies it was decided to administer 250 mg. of Aureomycin 30 minutes to one hour prior to breakfast and again two hours following the evening meal. In this manner 500 mg. were ingested daily on an empty stomach. Four hospitalized individuals who were subjected to this regimen disclosed blood levels ranging from 0.12 to 2.0 micrograms per milliliter during a period of 24 hours. No evidence of the antibiotic could be demonstrated in one case. Twelve ambulatory patients being followed through the Out-Patient Department also received this medication and revealed blood levels varying from 0.06 to 4.0 micrograms per milliliter over a period of 16 hours. Aureomycin could not be demonstrated in two instances. A review of the literature and our own in vitro studies suggested that these concentrations should forestall a significant percentage (perhaps the majority) of common respiratory and urinary tract infections.[12, 19, 20] Extensive clinical observations had indicated that this dosage produced minimal untoward effects. Therefore, this regimen (500 mg. daily) was adopted for the present investigation. Only Aureomycin containing Paraben was employed.

To eliminate unintentional prejudice and thereby obtain as objective results as possible, placebo capsules † were secured which were identical with the Aureomycin preparation. In this manner a control group of subjects was obtained who could be observed for comparative purposes. Neither the patient nor the physician knew which preparation a given individual was receiving.

Two hundred and four persons who were regularly attending the Diabetic Clinic of the John Gaston Hospital and the University of Tennessee College of Medicine were included in this investigation. All were from the lowest social and economic strata. Because of their failure to return to the clinic, 15 cases could not be followed. Of the remaining 189, 94 were in the Aureomycin group and 95 were in the control series. The average age of those in the antibiotic category was 55.2 years, as compared with 56.4 years for the controls. Seventy-seven of the patients in the Aureomycin series were Negroes and 17 were white; 79 of those in the placebo group were Negroes and 16 were white. In the Aureomycin category 23 were males and 71 were females, as compared with 21 males and 74 females among the controls. Definite cardiac disease was present in 31 instances. The etiology of this complication in the antibiotic group was as follows: hypertensive cardiovascular disease, 7; coronary artery disease, 5; hypertensive cardio-

* All medication employed in this study was supplied through the courtesy of the Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.

† The formula for the placebo capsules expressed as milligrams per capsule was anhydrous dicalcium phosphate, 689; magnesium stearate, 10; mineral oil, 13; F.D. and C. Yellow No. 5 dye, 1. Subsequently, this formula was altered to anhydrous dicalcium phosphate, 360; "proflo," 360; magnesium stearate, 10, and mineral oil, 10.

vascular disease and coronary artery disease, 3. A similar review of the control cases revealed: hypertensive cardiovascular disease, 8; coronary artery disease, 5; hypertensive cardiovascular disease and coronary artery disease, 2; rheumatic heart disease with mitral stenosis, 1.

Each patient in this study was examined at intervals of from two weeks to three months in the Diabetic Clinic of the John Gaston Hospital. In addition, every three months a comprehensive examination was performed in the Antibiotic Clinic. At that time the following laboratory procedures were carried out: hematocrit, sedimentation rate, complete blood cell count, urinalysis, nonprotein nitrogen, serum bilirubin, bromsulfalein retention, cephalin-cholesterol flocculation, total and fractional protein, cholesterol and cholesterol esters. Catheterized urine specimens were obtained for bacteriologic examination as frequently as possible. Electrocardiograms and roentgenograms were secured as indicated.

Results

The period of observation in this study ranged from four to 21 months, with an average of 19.5 months. Three deaths occurred during this investigation, one in the Aureomycin and two in the placebo categories. All of these fatalities occurred in the John Gaston Hospital and were carefully observed. All were admitted in coma; in no instance was a necropsy obtained. The single death in the Aureomycin series is briefly presented.

This case was that of a 75 year old Negro female who had been a known diabetic for 10 years. She was admitted to the Medical Service in diabetic coma of 24 hours' duration. Unconsciousness had resulted from failure to take insulin for approximately one week, even though the established daily dose was 40 units. Physical examination revealed hypertensive cardiovascular disease, auricular fibrillation and congestive failure. There was no evidence of respiratory infection as indicated by physical and roentgenologic methods. Despite intensive therapy employing insulin, fluids, electrolytes, digitalization and prophylactic antibiotics, consciousness was never regained. Death occurred 30 hours after hospitalization. Pertinent laboratory findings were as follows: white blood cell count, 16,000, with the differential cell count revealing polymorphonuclear leukocytes, 84 per cent, and lymphocytes, 16 per cent; hematocrit, 39 ml. per cent; hemoglobin, 11 gm. The initial urinalysis disclosed 3 plus proteinuria, 4 plus glucosuria, strongly positive acetone, red blood cells too numerous to count, but no white blood cells (centrifuged specimen); the initial blood sugar, 393 mg. per cent; chlorides, 505 mg. per cent, and carbon dioxide combining power, 6 vol. per cent.

The two fatal cases which occurred in the control group were Negro females, aged 51 and 57 years, respectively. In one instance coma followed irregular and inadequate insulin therapy, together with extreme dietary indiscretion for five days. Upon admission of the patient to the hospital coma had been present for 30 hours and was associated with peripheral vascular collapse and anuria. Despite adequate treatment, death occurred 12 hours after hospitalization. The second fatality in the control series was a 51 year old diabetic female who had been treated in the Out-Patient Department for

nine years; death resulted from miliary tuberculosis which precipitated irreversible coma.

The incidence of respiratory infections was definitely reduced in those patients receiving Aureomycin prophylactic therapy as compared with the controls (table 1). In the antibiotic group, infections involving the respiratory tract were reduced at least 50 per cent in 51 cases, were not significantly altered in 39, and were more frequent in four. A similar evaluation of the placebo category disclosed a decrease of 50 per cent or more in 20 instances, no significant alteration in 66, and an actual increase in nine. Therefore, approximately two and one-half times as many persons sustained a definite reduction in the respiratory infections in the Aureomycin group as in the controls. In line with these results was the observation that only

TABLE I

INCIDENCE OF RESPIRATORY INFECTIONS

SERIES	FEWER*	NO CHANGE	MORE
Aureomycin	51	39	4
Control	20	66	9

* These cases showed a reduction of at least 50% in the incidence of respiratory infections.

one hospitalization was necessary in the antibiotic series because of bronchopneumonia, as contrasted with three in the placebo group.

The diagnosis of a urinary tract infection in diabetic patients is often quite difficult. The underlying condition, especially if poorly controlled, may itself produce such symptoms as polyuria, nocturia and slight dysuria. Three patients in the Aureomycin group were believed clinically to have a urinary infection. In one case, symptoms were present at the onset of Aureomycin prophylaxis but disappeared within a week. A urinalysis prior to treatment was negative. However, a culture of this catheterized specimen yielded *Aerobacter aerogenes* (2 plus). No additional treament was administered, yet subsequent urinalyses and cultures were negative. In the two remaining instances physical examination was suggestive but equivocal; urinalyses disclosed pyuria in both cases. Bacteriologic cultures employing blood agar and eosin-methylene blue (Difco) plates yielded organisms

in only one instance. The latter patient revealed white blood cells too numerous to count in a centrifuged urine specimen, and bacteriologic examination disclosed both *Escherichia coli* and *Streptococcus pyogenes*. Even though this individual had already received 500 mg. of Aureomycin daily for three and one-half months, dosage was increased to 2 gm. daily for 14 days. After seven days, both cultures and urinalyses became persistently negative. The second patient disclosed pyuria but no organisms could be cultured; no additional therapy was administered, yet subsequent urinalyses were normal. In the placebo series, eight subjects were believed to have signs and symptoms of urinary disease. Microscopic examination of centrifuged urine disclosed pyuria in every instance, and cultures of catheterized

TABLE II

INCIDENCE OF PYURIA

	NO. OF PATIENTS	
	Aureomycin Series	Control Series
Transient Pyuria	19 (20 %)	21 (22 %)
Persistent Pyuria	15 (16 %)	19 (20 %)
Persistently Negative	60 (64 %)	55 (58 %)

specimens were positive in five cases but negative in three. The following organisms were isolated: *E. coli* (3), *Ps. aeruginosa* (1) and *A. aerogenes* (1).

A routine urinalysis was obtained on each patient every three months in the Antibiotic Clinic. Pyuria was observed to occur less often in the Aureomycin group than in the controls (table 2). However, this difference in incidence was not significant. Bacteriologic results in the two categories, however, were quite interesting. Before the initiation of prophylactic Aureomycin, catheterized specimens were obtained from 10 asymptomatic patients included in the antibiotic group. Organisms were isolated in six instances; four were negative. In the placebo series six similar specimens were studied; three were positive and three were negative. The organisms demonstrated in the Aureomycin patients were: *E. coli* (4), *A. aerogenes* (1) and *P. vul-*

garis (1). No additional medication aside from the routine 500 mg. of Aureomycin daily was administered; however, a repeated culture three months later was nonrevealing in all but one case (*E. coli*). The bacteria isolated initially from the control cases were *E. coli* (2) and *Ps. aeruginosa* (1). Repeated cultures at three month intervals continued to reveal these organisms for 18, 12 and 18 months, respectively.

During the course of this study 36 catheterized urine specimens were obtained at random from asymptomatic Aureomycin patients. Eight of these (22 per cent) were found to be positive, while 28 (78 per cent) were negative. In one instance *Candida albicans* (Monilia) was isolated; this patient had been receiving Aureomycin for five months. No follow-up urine study could be obtained. The bacteria demonstrated in these eight cases were *E. coli* (3), *P. vulgaris* (1), *Micrococcus pyogenes* var. *aureus* (3), *M. citreus* (1), and *Str. pyogenes* (1). In two instances previous cultures had revealed no microörganisms. Two of the three strains of *M. pyogenes* var. *aureus* were hemolytic. One of the patients yielding this organism had been demonstrated to have a negative urine prior to therapy, and again after 11 months of Aureomycin prophylaxis; however, at 15 months a hemolytic strain of *M. pyogenes* var. *aureus* was isolated. Although no change was made in treatment, a subsequent culture at 19 months was negative. The other case yielding a hemolytic strain moved from the Memphis area and could not be observed further. Twenty-eight random specimens were similarly obtained from asymptomatic placebo cases during the course of this study. Twelve of these (43 per cent) were positive. The organisms isolated were: *E. coli* (5), *A. aerogenes* (3), *Ps. aeruginosa* (1), *M. pyogenes* var. *aureus* (2) and *Str. viridans* (2). One of the strains of *M. pyogenes* var. *aureus* was hemolytic.

Accompanying the reduced incidence of respiratory and urinary infections in the antibiotic series was a slight reduction in the number of hospitalizations required by these patients. Hospitalization was necessary on 33 occasions in the control series, as compared with 31 in the antibiotic group. The total number of institutional days in the former category was 552, as compared with only 303 in the antibiotic category. Serial sedimentation rates (Wintrobe, corrected; Rourke-Ernstene technic) were performed at intervals of three months and disclosed no consistent difference of significant degree between the two groups of patients (figure 1). These laboratory findings could not be readily correlated with the reduced incidence of respiratory and urinary tract infections in those patients receiving antibiotic medication.

During the last three months of this investigation every patient was asked if he believed that his state of health had improved, had remained unchanged or had become worse since the present program was begun (table 3). In the Aureomycin group 66 believed themselves better, 29 had noted no change, and two regarded themselves as worse. Similar questioning of the placebo patients established that 28 believed themselves better, 57

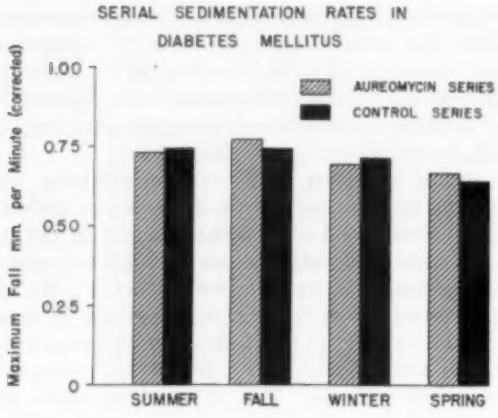


FIG. 1.

regarded their health as unchanged, and 10 considered themselves worse. Subjective opinions are extremely difficult to evaluate. However, all of the patients included in this project thought themselves to be receiving identical medication, and the examining physician had no information as to what preparation any individual was given. Therefore, it would appear that these opinions should be of value. Furthermore, the extended duration of this investigation should have eliminated early psychologic improvement resulting from the use of new medication.

After the first six months of therapy it was decided to investigate the possible effects resulting from the addition of minerals and multivitamins

TABLE III

SUBJECTIVE OPINIONS OF PATIENTS FOLLOWING PROPHYLACTIC THERAPY

SERIES	BETTER	NO CHANGE	WORSE
Aureomycin	63	29	2
Control	28	57	10

to the preparation being received by both categories of patients. This decision was a consequence of observations made in a large group of elderly patients with chronic congestive failure.[21] These cardiac patients noted a significant increase in appetite, strength and energy on Aureomycin. Furthermore, their hematocrit determinations revealed a definite increase. Similar manifestations had also been reported in a number of chronic respiratory cases.[22] Additional nutritional studies were believed indicated. Therefore, special capsules of a different color (blue) were obtained * and were substituted for the previous yellow ones.

Repeated hematocrit determinations disclosed a greater rise in the Aureomycin category (table 4). In this group there was an average increase

TABLE IV

HEMATOCRIT DETERMINATIONS

Series	No. Patients	Before Vitamin-minerals (6 mo)	After Vitamin-minerals (14 mo)	Over-all Results (20 mo)
Aureomycin	Increased	53	43	60
	No Change	9	10	8
	Decreased	32	34	26
	Ave. Increase	1.25 ml.%	0.60 ml.%	1.85 ml.%
Control	Increased	31	52	53
	No Change	20	17	15
	Decreased	44	6	27
	Ave. Increase	−0.25 ml.%	1.47 ml.%	1.22 ml.%

of 1.85 ml. per cent during this study, as contrasted with an increase of only 1.22 ml. per cent in the controls. These laboratory results corresponded well to the improved strength and energy frequently observed in the antibiotic subjects. A further evaluation of the hematocrit determinations revealed that prior to the addition of minerals and vitamins (that is, during the first six months of this project), there was an average increase in the

* The composition of the vitamin-mineral preparation added to both the Aureomycin and the placebo compounds was as follows per capsule: Vitamin A (as Acetate), 2500 U.S.P. Units; Vitamin D (Viosterol), 250 U.S.P. Units; Vitamin B_{12}–B_{12b}, 0.5 microgram as present in concentrated extractives from streptomyces fermentation; Thiamine HCl, 2.5 mg.; Riboflavin, 2.5 mg.; Niacinamide, 7.5 mg.; Folic Acid, 0.5 mg.; Pyridoxine HCl, 0.25 mg.; Ca Pantothenate, 2.5 mg.; Choline Dihydrogen Citrate, 50.0 mg.; Inositol, 25.0 mg.; Ascorbic Acid, 25.0 mg.; Vitamin E (as tocopherol acetates), 5.0 Units; Rutin, 12.5 mg.; Iron (as $FeSO_4$), 5.0 mg.; Iodine (as KI), 0.25 mg.; Calcium (as $CaHPO_4$), 72.5 mg.; Phosphorus (as $CaHPO_4$), 55.0 mg.; Boron (as $Na_2B_4O_7 \cdot 10H_2O$), 0.05 mg.; Copper (as CuO), 0.5 mg.; Fluorine (as CaF_2), 0.05 mg.; Manganese (as MnO_2), 0.5 mg.; Magnesium (as MgO), 0.5 mg.; Potassium (as K_2SO_4), 2.5 mg.; Zinc (as ZnO), 0.25 mg.

antibiotic category of 1.25 ml. per cent, as compared with an actual decrease of 0.25 ml. per cent in the placebo patients; during the ensuing 13.5 months, an average additional rise of 0.6 ml. per cent was recorded in the Aureomycin series and 1.47 ml. per cent in the controls. The antibiotic itself, therefore, appeared to be the most important factor in the improved hematocrit determinations in the Aureomycin cases. It is of interest to note that approximately 85 per cent of patients in both categories preferred the preparations containing vitamins and minerals. It was the widespread opinion that the latter resulted in more energy and in a sense of well being. Since the capsules with vitamins were much larger and more difficult to swallow than the previous ones, this preference would appear to be of significance.

TABLE V

SIDE EFFECTS TO AUREOMYCIN PROPHYLACTIC THERAPY

	NO. OF PATIENTS	
	Aureomycin Series	Control Series
NAUSEA	8	8
VOMITING	4	5
DIARRHEA	2 (mild)	0
PRURITUS ANI	3	0
PRURITUS VULVAE	4	4
INDIGESTION	0	3

Toxicity: With 500 mg. of Aureomycin daily, side effects were minimal (table 5). It was necessary to discontinue medication because of toxicity in one case in both categories. Nausea and vomiting were the complicating factors in each instance; following discontinuance of Aureomycin and the placebo compound all disturbing manifestations disappeared. Nausea occurred with equal frequency in both groups of patients. Vomiting actually was observed slightly more often in the control than in the antibiotic series. In one instance a patient noted mild nausea and vomiting with Aureomycin; however, this symptom did not recur when the Aureomycin-mineral-vitamin preparation was substituted. Of practical interest in geriatric patients with chronic illness was the observation that in 20 cases receiving Aureomycin, constipation was replaced by normal bowel habits. In the placebo group a similar effect was noted in six instances. However, a further evaluation of this alteration in bowel function revealed that improvement occurred in 15 patients in the Aureomycin series before minerals and vitamins were added,

as compared with only one in the placebo category. The importance of regular bowel habits to the elderly individual is generally appreciated by all internists.

All cases of diarrhea and pruritus ani reported in this study occurred in the antibiotic group. Fortunately, these complications were mild and transient, and required only symptomatic therapy. All patients were carefully instructed to observe strict hygienic measures; the importance of preventing anal irritation was stressed. Any evaluation of pruritus vulvae in diabetic individuals is, of course, somewhat difficult. No difference in the incidence of this symptom was observed in the two categories. However, in two instances discomfort was noted for the first time after two and one-

TABLE VI

LIVER FUNCTION STUDIES

DETERMINATION	SERIES	NO. OF CASES			
		Persistently Normal	Persistently Abnormal	Became Abnormal During Therapy	Showed Improvement During Therapy
BSP Retention	Aureomycin	39	15	12	13
	Control	33	19	14	13
Cephalin-cholesterol Flocculation	Aureomycin	86	0	0	8
	Control	86	1	3	3
Serum Cholesterol	Aureomycin	41	14	23	15
	Control	64	12	6	2
Serum cholesterol Esters	Aureomycin	25	32	19	27
	Control	24	24	18	34
Serum Bilirubin	Aureomycin	89	1	3	1
	Control	92	0	1	0
Serum Albumin	Aureomycin	71	3	6	14
	Control	64	4	23	3
Serum Globulin	Aureomycin	52	6	15	21
	Control	47	12	19	16

half and 16 months, respectively, of Aureomycin therapy. In neither case did discomfort persist more than 10 days. Symptomatic treatment was effective in each case.

Because of the possibility of deleterious effects resulting from the prolonged administration of Aureomycin, comprehensive liver function tests were carried out initially and thereafter at intervals of three months in both groups of patients (table 6). The importance of a battery of determinations in evaluating the various functions of this organ was well illustrated by the results obtained. Cholesterol esters were persistently abnormal in 37 cases (20 per cent), serum globulin in 34 (18 per cent), serum cholesterol in 29 (15 per cent), serum albumin in 29 (15 per cent), bromsulfalein retention (5 mg. per kg. of body weight in 45 minutes) in 26 (14 per cent), serum bilirubin in four (2 per cent), and cephalin cholesterol flocculation in

three (1.5 per cent). Serial determinations of the serum albumin, serum globulin and bromsulfalein retention as well as cephalin-cholesterol flocculation tests indicated greater improvement in the Aureomycin than in the control groups. On the other hand, values for the serum cholesterol and the cholesterol esters were generally more normal in the placebo category. Hepatic function studies performed during the first six months of this project were compared with those obtained later in an effort to evaluate the effect of minerals and multivitamins. During the terminal 13.5 months a definite improvement was observed in the Aureomycin series in cholesterol esters, serum albumin and serum globulin. Even more striking improvement in these tests was noted in the control patients. However, the values recorded for serum cholesterol in the placebo category became more abnormal during the latter portion of this study. The remaining laboratory procedures disclosed no significant difference before and after the addition of minerals and vitamins.

Bone marrow preparations were obtained in 20 patients; 10 of these were in the Aureomycin group and 10 were in the placebo group. No evidence of toxicity due to prolonged antibiotic therapy was observed. These studies were carried out in association with Dr. Alys Lipscomb, of the Department of Medical Laboratories, and will be reported in detail elsewhere.

Discussion

Life expectancy has become progressively greater in recent years. As a result of the larger proportion of elderly individuals in the general population, medical interest has increasingly tended to emphasize the diseases of later life. Today diabetes mellitus is a major medical problem. It has been estimated that 2 per cent of males and 4 per cent of all females under the age of 50 years now living in this country will eventually have diabetes mellitus.[3] Furthermore, it appears that during the next few years the number of diabetics will increase twice as rapidly as the general population. Despite remarkable advances in therapy, this condition rose from twenty-seventh in 1900 to eighth in 1940 among the causes of death in the United States.

Seven and eight tenths per cent of all fatalities in diabetic persons result from acute infections.[3] These individuals are especially prone to involvement of the urinary and respiratory systems. The rôle of infection in the management of diabetes mellitus is a well recognized but complicated one. In the presence of an inflammatory process the metabolic status of the body is deranged; adjustment of insulin therapy becomes quite difficult. Acidosis and coma may rapidly ensue. While the death rate resulting from coma has greatly decreased, it is still significant. That recent favorable mortality statistics may be somewhat misleading has been emphasized in a current review.[23] In the present investigation, three deaths occurred; all were associated with irreversible coma and its sequelae.

It is becoming increasingly apparent that infection plays an important direct and indirect rôle in the prognosis of diabetes. The greatest number of deaths in this condition result from degenerative side effects. A recent study established that the occurrence of cardiovascular renal complications could be reduced by long continued excellent diabetic control.[7] Excellent control is impossible, however, in the face of repeated bouts of infection. Therefore, excellent control in diabetes implies excellent control of infection. Diabetic nephropathy is the most common fatal complication occurring in young persons; histopathologic studies established that pyelonephritis is usually involved.[8] The etiology of necrotizing papillitis, a serious condition in diabetes, is also apparently associated with pyelonephritis.[9]

It occurred to us that prolonged antibiotic prophylaxis in diabetic patients might reduce the incidence of intercurrent infections. If respiratory and urinary diseases could be diminished, it would permit a longer, pleasanter and more useful existence. Inasmuch as Aureomycin is effective against many gram-positive and gram-negative organisms, and produces very few serious side effects, it was decided to employ this agent in a large series of cases. It should be emphasized that the goal of the present study was prevention, not cure. After a consideration of blood levels attained with various amounts of Aureomycin, the following daily regimen was selected: 250 mg. 30 minutes to one hour before breakfast, and again two hours after the evening meal.

One hundred eighty-nine diabetics were observed for an average of 19.5 months. One death occurred in the antibiotic category, two in the placebo group. The lone fatality in the former series was a 75 year old Negro female who became comatose because of failure to receive insulin for a week. The two control deaths were Negro females, aged 51 and 57 years, respectively. In one case coma followed dietary indiscretion together with inadequate insulin therapy; coma in the other instance was precipitated by miliary tuberculosis.

A reduction of respiratory infections by at least 50 per cent occurred in two and one-half times as many persons in the Aureomycin group as in the placebo series. Likewise, pyuria was demonstrated less often in the antibiotic than in the control cases. This difference, however, was not significant. Only two patients in the Aureomycin series presented signs and symptoms of an acute urinary infection during this study, as contrasted with eight in the placebo group. While pyuria was present in all 10 of these cases, bacteria could be cultured from only one antibiotic patient and five controls.

One of the most perplexing problems in the management of diabetes mellitus is the proper handling of urinary infections. The importance of prompt and adequate therapy is well recognized. Unfortunately, symptoms are often minimal or absent. Therefore, urinalyses should be performed at regular intervals in all instances. With this in mind, 36 catheterized specimens were obtained at random from asymptomatic Aureomycin patients;

eight of these (22 per cent) revealed bacteria, while 28 (78 per cent) were negative. Similarly, 28 random specimens in the placebo category revealed 12 (43 per cent) positive, while 16 (57 per cent) were negative. Of interest is the fact that two hemolytic strains of *M. pyogenes* var. *aureus* were isolated in the Aureomycin series as compared with one in the controls. It was impossible to follow one of the antibiotic cases yielding this organism, but in the second case a subsequent culture was negative though treatment had not been altered.

The reduction in intercurrent infections in the antibiotic patients was not accompanied by a significant alteration of the sedimentation rate. Serial hematocrit determinations revealed a greater increase in those receiving Aureomycin prophylaxis. After the first six months of this investigation, minerals and multivitamins were added to both the Aureomycin and the placebo preparations. During this initial period the average hematocrit actually decreased in the controls while substantially rising in the Aureomycin group; after the administration of minerals and vitamins, a definite increase occurred in the control group. A further, less significant rise was also recorded in the antibiotic series. These findings indicate the importance of supplementary vitamins and minerals in diabetic individuals who are being maintained on a restricted diet; this statement undoubtedly could be extended to all patients having a limited nutritional intake. Nonetheless, a consideration of the over-all figures establishes that Aureomycin was the important factor in the greater hematocrit increase recorded in the antibiotic patients. This improvement would appear to be the result of fewer infections. That anemia is frequently encountered in diabetes has been reported.[3]

Since the patients included in this study believed that the medication administered to every one was identical, and since the examining physician was unaware of which preparation an individual was receiving, the subjective opinions of those treated should be significant. In the Aureomycin group 66 considered themselves better, as compared with only 28 of the controls; in the former category two regarded themselves as worse, while this impression was reported by 10 in the placebo category.

With the dosage of Aureomycin employed in this study, side effects were minimal. Nausea and vomiting necessitated the discontinuance of therapy in two cases, one in each category. There was no significant difference in the incidence of these annoying complaints in the two groups of cases. The importance of a placebo substance in the evaluation of toxicity cannot be minimized. On two occasions physicians reported nausea and vomiting apparently due to antibiotic therapy; both patients were subsequently found to be controls. When a patient has gastrointestinal symptoms while taking a broad spectrum antibiotic there is a great tendency to assume that the drug must be responsible. Pruritus ani and diarrhea occurred exclusively in the antibiotic group. Both of these complications were infrequent, transient and mild.

Comprehensive liver function studies revealed no evidence of toxicity resulting from prolonged antibiotic therapy. Indeed, there was some evidence of an improved hepatic state. Bone marrow preparations failed to disclose any abnormality related to prophylactic therapy. While no specific efforts were made in the present investigation to evaluate the development of bacterial resistance in long term Aureomycin treatment, this problem was extensively considered in associated studies.[21, 22, 24] This would not appear to be a common difficulty. It is interesting to note that in the present project a urinary tract infection and a perirectal abscess occurred in two Aureomycin patients. Both responded excellently when dosage was increased to 2 gm. daily.

Summary

The control of intercurrent infections in diabetes mellitus is essential for good management and a favorable prognosis. Therefore, prolonged antibiotic prophylaxis was believed to warrant investigation.

Ninety-four patients having diabetes mellitus received 500 mg. of Aureomycin daily for an average of 19.5 months; 95 similar cases received an identical placebo compound and were followed for comparative purposes. A definite reduction in urinary and respiratory infections was observed in the antibiotic group. This decrease in secondary infections correlated quite well with the results of comprehensive laboratory procedures, which indicated a better state of health in the antibiotic patients. In addition, a subjective feeling of improvement was more frequently reported by those receiving Aureomycin. Toxic manifestations were minimal. Using Aureomycin with Paraben, *C. albicans* (*M. albicans*) produced no serious problem.

Additional studies concerning the development of bacterial resistance are necessary. Nonetheless, it appears that prolonged antibiotic prophylaxis may be of value in the management of diabetes mellitus.

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EMPYEMA AS A COMPLICATION OF BLAND PULMONARY INFARCTION: CONSIDERATION OF THE PROBLEM AND REPORT OF FIVE CASES*

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"WHILE simple infarcts caused by aseptic thrombosis or embolism may occasionally become infected by inhaled bacteria and go on to abscess formation, such an event is notable for its infrequency." This statement was made by Dr. J. Burns Amberson in the Thayer Lectures delivered at the Johns Hopkins University in 1953.[1]

In a series of 550 cases of bland pulmonary infarction reported from the Mayo Clinic, pulmonary abscess occurred in 4.2 per cent and empyema in 1.1 per cent.[2] Although there are several reports in the literature of empyema following bland pulmonary infarction, the number is small.[2, 3, 4, 5] Particularly striking is the high mortality rate among the reported cases. For these reasons five such cases of empyema recently encountered which were promptly treated by surgical drainage with good results are presented in the present communication.

Between 1949 and 1952, five individuals admitted to the wards of the Johns Hopkins Hospital with bland pulmonary infarction subsequently developed empyema. Following is a summary of these cases:

CASE REPORTS

Case 1. A 60 year old laborer entered the hospital complaining of pain in the right chest, cough and hemoptysis of one day's duration. Six weeks before he had sustained a fracture of the right femur treated by open reduction and immobilization. He was in good physical condition, although he had mild hypertension. There was no evidence of phlebitis in either leg. Although he was febrile on admission, his temperature became normal following penicillin therapy. Dicumarol was administered. However, 12 days following the infarction fever reappeared, with evidence of right pleural effusion. Multiple thoracenteses did not alter his course, and on the thirty-seventh day an empyema cavity was found on aspiration. *Clostridium novyi* was cultured from the thick purulent material obtained. The patient had become quite severely ill with high fever, profuse sweats and severe malaise. Immediate rib resection with adequate open drainage was instituted. His temperature returned to normal and recovery was rapid. He has since remained well.

Case 2. A 39 year old male entered the hospital for treatment of a duodenal ulcer. The operation was performed. On the third postoperative day he had sudden onset of crushing substernal pain, followed by shock and pulmonary edema. The electrocardiogram showed changes compatible with a posterior myocardial infarction.

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Following this there was left thoracic pain accompanied by suppression of breath sounds over the left lower lobe. He had hemoptysis and fever and became desperately ill. The clinical diagnosis was infarction of the left lower lobe, secondary to an embolus from a mural thrombus of the infarcted myocardium. His condition became critical, with high fever. Twenty-eight days following the pulmonary infarction, thick yellow pus was obtained on aspiration of the left chest. This contained *Bacteroides funduliformis*. Closed drainage was employed for seven days, but without success. Although the patient's condition was poor, adequate open surgical drainage was accomplished by rib resection. He completely recovered and returned to work.

Case 3. A 50 year old female with severe hypertension of long duration entered the hospital critically ill. Four days prior to admission she had had pain in the right chest, fever, cough and hemoptysis. She had severe cardiac failure and signs of pulmonary infarction in the right lower lobe. Anticoagulants and penicillin were administered. The patient remained critically ill. Four weeks following admission, signs of pleural effusion developed over the right chest and a thoracentesis was performed. Thick pus infected with a nonhemolytic *Staphylococcus aureus* was obtained. Open surgical drainage was established by rib resection. The patient rapidly improved and has remained well.

Case 4. A 40 year old female who had rheumatic heart disease with mitral stenosis and insufficiency and fibrillation was admitted in severe congestive failure. Four days after admission she had severe pain in the right chest and coughed up bloody sputum. A film of the chest revealed a shadow in the right lower lobe consistent with the diagnosis of pulmonary infarction. Her condition became critical at this time. On the fifty-seventh day after her pulmonary infarction her temperature rose abruptly. A thoracentesis was performed and thick creamy pus containing a hemolytic *Staphylococcus aureus* was obtained. Penicillin was given, but the fever continued. Aspiration drainage of the empyema was attempted for five days, with little success. Although the patient was desperately ill, open drainage of the empyema was instituted by rib resection. The temperature dropped to normal within four hours. The patient died suddenly on the second postoperative day. At autopsy it was evident that there was occlusion of the mitral valve by a ball valve thrombus from the left auricle. There were no fresh pulmonary infarcts. The empyema cavity had been well drained.

Case 5. A 45 year old female who had hypertension was admitted in severe cardiac failure and with encephalopathy. On her fifth hospital day she had sudden onset of cough, hemoptysis, fever and severe pain in the right chest. The following day the right great saphenous vein became tender, and the right leg measured 2 cm. more than the left at all points. Penicillin and Dicumarol were given. During the next 10 days she had repeated pulmonary emboli, with accompanying signs and symptoms of infarction. Bilateral superficial venous ligation in the legs was performed, but the emboli continued to occur. A month later signs of pleural effusion developed, with a rapid rise in temperature. Aspiration of the chest revealed pus containing *Staphylococcus aureus* and an alpha-hemolytic streptococcus. The patient's condition was precarious. Rib resection with open drainage was performed. The fever promptly subsided, and the cardiac failure improved. She recovered and has remained well.

Pulmonary infarction occurs most frequently when heart failure is present.[6] Such patients are almost always critically ill from the underlying cardiovascular disorder in addition to the infarction. Four of the five patients in this report had cardiac failure of severe degree at the time of the pulmonary infarction. One had had a myocardial infarction, another had

TABLE I

Empyema in Five Patients with Bland Pulmonary Infarction

Patient	Age	Sex	Type of Heart Disease / Presence of Failure	Location of Infarction	Source of Embolus	Symptoms and Signs					Effusion	Time after Infarction Empyema Was Proved	Cultures		Treatment	Result
						Pain	Cough	Hemoptysis	Fever	Leukocytosis			Sputum	Empyema Fluid		
C. H.	50	F	Hypertensive heart disease / +	RLL	Presumed mural thrombus	+	+	+	+	+	−	24 days	Normal flora	Nonhem. *Staph. aureus*	Penicillin and partial resection R 10 and 11 ribs	Good
M. H.	45	F	Hypertensive heart disease / +	LUL RML RLL	Right great saphenous vein	+	+	+	+	−	+	34 days	Alpha strep.	Nonhem. *Staph. aureus*	Penicillin and partial resection R 10 rib	Good
C. H.	60	M	Hypertensive heart disease / −	RLL	Right leg (cast)	+	+	+	+	−	+	37 days	Alpha strep.	*Clostridium novyi*	Penicillin and partial resection R 8 and 9 ribs	Good
T. S.	39	M	Myocardial infarction / +	LLL	Presumed mural thrombus	+	+	+	+	+	+	28 days	Alpha strep.	*Bacteroides funduliformis*	Penicillin Aureomycin Gantrisin and partial resection L 8 and 9 ribs	Good
R. B.	40	F	Rheumatic heart disease / +	RLL	Right auricular thrombus	+	+	+	+	−	+	57 days	Alpha strep.	Hemolytic *Staph. aureus*	Penicillin and partial resection R 10 rib	Dead*

* Autopsy—Ball valve thrombus occluding mitral valve.

rheumatic heart disease with mitral valvulitis and auricular fibrillation. A third had hypertensive cardiovascular disease, and a fourth severe hypertensive cardiovascular disease with phlebitis in the right leg. The fifth patient had mild hypertension with good cardiac function. There were presumably deep venous thrombi in his legs resulting from prolonged immobilization for a fractured femur.

Pulmonary embolism is most common in the right lower lobe and in this particular group the infarction occurred in the right lower lobe in four of the five patients. The signs and symptoms followed the classic pattern. Thoracic pain, fever, cough and hemoptysis were present in each instance, but leukocytosis was present in only two out of five. Sterile pleural effusion occurred in three of the patients, necessitating repeated thoracenteses. The empyema which occurred in these five patients was in each case a localized one. Characteristically it occurred late in the course of the illness (24 to 57 days). This complication interrupted a course of progressive improvement and was not related to the last pleural tap on those three patients who had had a sterile effusion in association with the pulmonary infarction. There was no evidence that these patients had had pneumonia. Cultures of the sputum of each patient failed to show pneumococci or the specific organism cultured from the empyema. The onset of empyema was preceded by increase in malaise, reappearance of fever and leukocytosis and, in three of the five patients, recurrence of severe cardiac decompensation.

The aspiration of pus from the localized area in the thoracic cavity established the diagnosis of empyema in each instance. The definitive therapy in each of these cases was drainage of the empyema by resection of one or two ribs and the institution of open drainage with large drainage tubes in conjunction with the administration of penicillin. It should be emphasized that, despite the fact that these patients were critically ill and three remained in congestive failure, effective treatment could be obtained only by immediate institution of adequate surgical drainage. It was this approach that resulted in the recovery of four of the patients here reported. The fifth patient died and at autopsy it was found that a ball valve thrombus had occluded the mitral orifice. This was not thought to be associated with the operative procedure.

Summary

1. Empyema in bland pulmonary infarction has been considered a rare complication. Five cases of this disorder have been observed in the Johns Hopkins Hospital in the past three years.

2. The association of preëxisting cardiovascular disease and the general critical condition of such patients is emphasized.

3. The most successful approach to this problem is the institution of immediate adequate surgical drainage of the empyema in conjunction with chemotherapy. This resulted in the recovery of four of the patients.

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EFFECT OF HEPARIN ON PLASMA LIPID PARTITION IN MAN: STUDIES IN NORMAL PERSONS AND IN PATIENTS WITH CORONARY ATHEROSCLEROSIS, NEPHROSIS AND PRIMARY HYPERLIPEMIA*

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This study is concerned with the effect of heparin on plasma lipid partition in man under normal and certain pathologic conditions. That heparin reduces the opacity of lipemic blood plasma has been demonstrated in several laboratories. While some observations have been made on individual plasma lipids after heparin administration,[6-10] comprehensive studies of plasma lipid partition in normal persons and in disturbances associated with lipemia are almost wholly lacking. In this investigation the effect of heparin on plasma lipids was observed in 25 subjects in four groups consisting of 10 normal men, five patients with coronary atherosclerosis, seven with nephrosis and three with idiopathic hyperlipemia.

Procedure

After a fasting blood specimen was obtained each subject was given an intravenous injection of a measured dose of heparin. Blood samples were drawn again 15, 60 and 120 minutes later. Plasma opacity was then determined by light transmission in a Coleman spectrophotometer set at 650 mμ. This was done for each subject soon after the two hour specimen was obtained. In a period of two to three hours of standing there was no appreciable change in turbidity of heparinized plasma. Timing of the readings of light transmission was kept uniform for all groups.

Quantitative determinations were made on all plasma specimens for total lipids (Bloor method), cholesterol and esterified cholesterol (Sperry-Schoenheimer method), and phospholipids (Sperry's modification of the Fiske-SubBarow method). Neutral fat was calculated by subtracting the figures for total cholesterol plus phospholipid from the figure for total fat, a procedure which has also been used by others.[1, 2]

Since we wished to make all our observations on plasma we used oxalate rather than heparin to prevent clotting of the pre-heparin blood sample, which made it necessary to use oxalate in all specimens. Oxalated plasma contains significantly smaller amounts of total and free cholesterol and phos-

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From the Departments of Medicine and Chemistry, Mt. Sinai Hospital. This investigation was supported in part by a research grant from the Division of Research Grants and Fellowships, National Institutes of Health, United States Public Health Service.

pholipid and perhaps total lipid than either serum or heparinized plasma from the same blood sample.[3] However, its uniform use throughout the present study does not preclude a *comparison* of plasma lipid fractions, despite the fact that figures obtained in each determination represent less than the absolute value which might have been found without oxalate.

Groups I and IA contained 10 healthy male volunteers, two of whom were hospital employees. Eight were blood donors obtained with the coöperation of the Blood Transfusion Association of New York. They ranged in age from 22 to 42 years and had no symptoms or stigmata of atherosclerosis. Five members (Group I) were given heparin in the fasting state, while the remaining 5 (Group IA) received heparin after alimentary lipemia was induced with a standard fat-loading test meal consumed three hours earlier.[4] The meal consisted of a measured quantity of heavy cream supplying 1 gm. of fat per kilogram of body weight, a slice of toast and a cup of tea. The dose of heparin * was 25 mg.

Group II was composed of four men and one woman, 39 to 67 years old. They were hospitalized patients with coronary atherosclerosis recovering from typical attacks of acute myocardial infarction and were not receiving anticoagulant medication. Each was given 25 mg. of heparin after an all-night fast.

Group III was made up of ward patients, four females and three males, in the nephrotic stage of nephritis. In most of them the fasting plasma appeared opaque ("milky"). There were three children, aged four, seven and 12 years, and four adults, 30 to 65 years old. Clinical data concerning these patients are given in table 1. All were in the fasting state when heparin was given. The adults received initially 25 mg. of heparin, while doses given to the three children varied with age and weight and were calculated on the basis of 25 mg. for an adult of 150 pounds body weight. In three patients the tests were repeated after a lapse of a week or more with larger doses to determine a possible relation between dosage and heparin effect.

Group IV comprised three subjects: a four year old girl with idiopathic hyperlipemia; a 44 year old man suffering with gout, who five years before had had an attack of nephritis but whose kidney function was now apparently normal while his blood serum remained markedly turbid; and a 46 year old apparently healthy man who a year before had discovered that his blood serum was milky. The child was given 10 mg. of heparin, the adults 25 mg. and 100 mg., respectively, all in the fasting state. Their clinical data also appear in table 1.

Effect on Plasma Transparency

In nearly every instance plasma obtained 15 minutes after heparin injection showed an increase in transparency. The clearing effect was also

* Liquaemin solution, Organon, Inc., N. J., 1 c.c. = 1,000 U. S. P. units of heparin, equivalent to 10 mg.

TABLE I

Clinical Data of Patients with Nephrosis and Idiopathic Hyperlipemia (Groups III and IV)

Subject	Age	Sex	Urine Albumin	Albuminuria 24 hrs. gm.	Casts	R.B.C.	Total Serum Protein (gm. per 100 ml.)	Serum Albumin (gm. per 100 ml.)	Serum Globulin (gm. per 100 ml.)	Blood Urea Nitrogen mg. per 100 ml.	Serum Cholesterol mg. per 100 ml.	Chlorides mEq./L.	Sodium mEq./L.	Potassium mEq./L.	Sedimentation Rate*	Blood Pressure
Nephrosis																
R. M.	4	M	4+	6	+	+	4.4	1.3	3.1	41	900	106	124	4.5	134	110/70
R. F.	7	M	4+	7	+	+	5.1	1.0	4.1	12	1460	104	138	4.5	120	128/65
R. McK.	12	F	4+	4	+	+	5.1	1.2	3.9	16	750	109	190	4.1	115	150/90
G. T.	30	F	4+	4	+	+	5.3	1.4	3.9	8	650	110	134	4.7	130	150/100
P. Z.	35	M	4+	9.3	+	+	3.5	1.2	2.3	92	600	106	143	6.0	95	190/110
R. K.	46	F	2+	5.4	+	+	6.0	2.3	3.7	14	850	107	149	4.9	120	178/110
J. G.	65	F	3+	–	+	+	8.2	3.7	4.5	52	347	110	91	3.4	128	162/92
Idiopathic Hyperlipemia																
C. G.	4	F	Ft. trace				7.7	4.1	3.6	14					21	96/70
S. Z.	44	M	0		0	0					Nonprotein N 33 mg. per 100 ml. Normal creatinine and inulin clearance. PSP 65% in 2 hours					Normal
M. M.	46	M	0				7.6	4.2	3.4		Asymptomatic. Hyperlipemia discovered 1 year ago					152/92

* Westergren method. Values express mm. sedimentation in one hour.

evident in the plasma specimens 60 and 120 minutes after heparin. Opacity of plasma was related only in a general way to its total lipid and neutral fat content. Although high total lipid values were usually associated with

TABLE II

Light Transmission (% at 650 mμ) of Plasma before and after Heparin

Subject	Age	Mg. of Heparin	Fasting	15 Minutes * after Heparin	1 Hour * after Heparin	2 Hours * after Heparin
Group I. Normals						
A. M.	25	25	31	74 (+43)	84 (+53)	74 (+43)
L. A.	27	25	63	68 (+ 5)	75 (+12)	68 (+ 5)
C. S.	28	25	45	49 (+ 4)	62 (+17)	64 (+19)
C. D.	36	25	52	70 (+18)	66 (+14)	61 (+ 9)
J. B.	38	25	63	75 (+12)	71 (+ 8)	73 (+10)
Group II. Atherosclerosis						
C. N.	39	25	38	53 (+15)	80 (+42)	77 (+39)
R. M.	52	25	30	60 (+30)	50 (+20)	37 (+ 7)
L. Z.	53	25	72	76 (+ 4)	81 (+ 9)	84 (+12)
J. S.	63	25	60	72 (+12)	72 (+12)	80 (+20)
N. P.	67	25	84	86 (+ 2)	80 (− 4)	79 (− 5)
Group III. Nephrosis						
R. M.	4	10	75	76 (+ 1)	62 (−13)	39 (−36)
R. F.	8	10	—	12.5	16.5	15
R. McK.	12	15	46.5	70 (+23.5)	66 (+19.5)	55 (+8.5)
R. McK.	12	35	32	40	41	50
G. T.	30	25	76	79 (+ 3)	79 (+ 3)	77 (+ 1)
P. Z.	35	25	16	21 (+ 5)	29.5 (+13.5)	40 (+24)
P. Z.	35	75	30	60	71	69
P. Z.	35	100	76	80	76.5	67
R. K.	46	25	71.5	71 (−.5)	71 (− .5)	69 (−2.5)
J. G.	65	50	5†	7.5	8	12.5
J. G.	65	100	7†	10	12	17
J. G.	65	150	21.5†	27.5	34	38.5
Group IV. Idiopathic Hyperlipemia						
C. G.	4	10	25	31 (+6)	38 (+13)	38 (+13)
S. Z.	44	25	19†	21 (+2)	32 (+13)	38 (+19)
M. M.	46	100	11	2.5 (−8.5)	2.5 (−8.5)	4 (− 7)
Mean Optical Density Expressed as Light Transmission (%)‡						
Group I	30.8		49	67 (+18)	71 (+22)	68 (+19)
Group II	54.5		53	68 (+15)	72 (+19)	69 (+16)
Group III	25.4		48	58 (+10)	58 (+10)	54 (+ 6)

* The figures in parentheses indicate the actual unit change as compared with the readings made on the fasting plasma. Increased (+) light transmission indicates increased translucency; decrease in light transmission (−) represents decreased translucency.

† All plasma specimens diluted 1:4 because of opacity.

‡ The figures were obtained by converting light transmission readings into equivalent optical densities. The mean optical density for each group is expressed in terms of light transmission in order to facilitate review.

marked opacity, occasionally plasma with a similar lipid content gave disparate spectrophotometric figures. For example, light transmission readings of 30 and 76 per cent were obtained with two different plasma specimens containing almost identical amounts of lipid, namely, 870 and 890 mg. per 100 ml., indicating that plasma total lipid and neutral fat do not alone determine plasma opacity.

Table 2 presents plasma light transmission readings for the four groups of fasted subjects. The calculated per cent change in light transmission is given in parentheses for subjects in Groups I, II and III who received comparable amounts of heparin, and for the three subjects of Group IV in whom other doses of heparin were used. Plus signs indicate clearing of lipemia as demonstrated by increased light transmission, whereas minus signs represent increased turbidity with diminution of light transmission. The mean light transmissions were calculated by converting the readings into their equivalent optical densities and averaging them. In a suspension the quantity of a substance (or the turbidity) is proportional not to the light transmission when read in the spectrophotometer, but to the optical density. The mean optical densities were then reconverted and expressed in terms of light transmission to facilitate comparison.

In each group there were wide variations in the degree of clearing. The total lipid concentration of the fasting plasma differed between the groups, the mean being 705 mg. for the normals, 911 mg. for the atherosclerotic patients and 2,065 mg. per 100 ml. for the nephrotic group. In the three individuals with idiopathic hyperlipemia the initial total plasma lipids were also quite high, namely, 895, 1,830 and 2,090 mg. per 100 ml. (tables 4, 5).

Plasma Clearing in Groups I, II and III: A comparison of the means given at the bottom of table 2 indicates that there were apparently some differences in clearing by heparin in normal subjects and patients with coronary sclerosis on the one hand, and in patients with nephrosis on the other. The clearing effected by heparin in the latter group was less than in Groups I and II. The standard deviation of the means, as calculated for small series, is high and does not permit definite conclusions. However, the figures are suggestive. Fifteen minutes after heparin the change in plasma light transmission of the nephrotic patients was plus 10, while that of the other two groups was plus 18 and plus 15. The relatively small amount of clearing of the nephrotic plasma as contrasted with that of the other groups was even more pronounced in the later test periods. After one hour the mean in Group III was 10 points above that of its fasting level, as compared with a 22 and a 19 point rise in Groups I and II. After two hours the corresponding mean changes were plus 6 for the patients with nephrosis in contrast with plus 19 and plus 16 for the other categories. The plasma of the nephrotic patient J. G. also showed little clearing after heparin injection, despite the fact that she received an initial dose of 50 mg., an amount twice as large as that given the other nephrotic patients. Because

of this larger dose and the fact that her opaque plasma had to be diluted with saline to permit a reading of transparency, a procedure not done for the others of Group III, her data are not included in the means of table 2.

Plasma Clearing in Group IV: In three patients with idiopathic hyperlipemia, injection of heparin did not produce any notable clearing of the plasma after 15 minutes. In two patients clearing of 13 to 19 points did occur after 60 and 120 minutes. The plasma of patient S. Z. was too opaque for any determination of light transmission and had to be diluted with physiologic saline in order to obtain readings in the spectrophotometer, a fact which probably reduced the dependability of the readings. In M. M., who received 100 mg. of heparin, an amount greater than was given to others in the group, no plasma clearing took place after heparin. The plasma of this patient was particularly opaque. In his undiluted plasma some clearing by heparin may have occurred without being detectable in the

TABLE III

Light Transmission (% at 650 mμ) of Plasma before and after Heparin
Normal subjects with induced lipemia (Group IA)

Subject	Age	Mg. of Heparin	Fasting	After Induced Lipemia	15 Minutes after Heparin	1 Hour after Heparin	No. of Points Clearing * after Heparin	
							15 mins.	1 hour
R. vL.	22	25	—	43	71	56	+28	+13
N. J.	26	25	68	30	57.5	67	+27.5	+37
T. B.	34	25	22	5	67	48	+62	+43
B. V.	41	25	10.5	12	47	50	+35	+38
G. A.	42	25	19	3.5	25	7.5	+21.5	+ 4
Means†	33	25		12	50	37	+38	+25

* See footnote * of Table II.
† See last footnote of Table II.

spectrophotometer. The sensitivity of the instrument in this end of the scale is limited.

Plasma Clearing of Alimentary Lipemia, Group IA: The rapid clearing effect of heparin in normal subjects was further demonstrated in five healthy individuals who were given heparin near the peak of induced postprandial lipemia (Group IA, table 3). Fifteen minutes after heparin their plasma cleared appreciably, with a mean rise in light transmission of 38 points. Since the postprandial peak of fat digestion occurs normally at about four hours, and sometimes even at six, injection of heparin three hours after a fat meal anticipated the peak by perhaps one to three hours. The prompt clearing after heparin injection must therefore be attributed largely to heparin and, to a lesser extent, to physiologic lipemia clearance. The average change in light transmission one hour after heparin was 25 units.

Relationship of Size of Dose to Degree of Clearing: After the lapse of a week, tests with larger dosages of heparin were repeated in three nephrotic

patients. Increased amounts of heparin did not produce any consistent enhancement of clearing effect. In R. McK. the clearing effect of 35 mg. of heparin was less pronounced than that of 15 mg. However, on the day the larger dose was given the lipemia was at a higher level (2,572 mg. per 100 ml.) than on the day when 15 mg. were given (1,775 mg. per 100 ml.). In a second patient (P. Z.), whose initial fasting plasma lipid levels at three different times were fairly similar, 100 mg. seemed to clear less than did 25

TABLE IV

Mean Plasma Total Lipid and Neutral Fat before and after Heparin (Groups I, IA, II, III) (mg. per 100 ml.)

	Total Lipids				Neutral Fats			
	Before Heparin	15 Minutes after Heparin	1 Hour after Heparin	2 Hours after Heparin	Before Heparin	15 Minutes after Heparin	1 Hour after Heparin	2 Hours after Heparin
Group I								
Means	705.0	646.0	606.0	666.0	315.4	250.2	209.8	271.8
S. D.	196.7	131.7	164.4	133.3	134.4	70.5	86.3	77.2
Group IA								
Means	760.0	640.0	648.0	—	283.2	193.4	208.4	—
S. D.	194.1	146.4	118.6	—	136.6	100.1	94.3	—
Group II								
Means	911.0	718.8	859.0	792.0	386.2	246.3*	330.8	290.8
S. D.	28.9	97.1	210.0	172.0	166.3	72.9	121.9	51.0
Group III								
Means	2065.7	1832.1	1763.6	1674.3	838.2	778.6	737.7	630.5
S. D.	966.9	677.3	589.2	569.1	405.6	379.8	353.6	307.5
	Per Cent Change from Fasting Level after Heparin							
Normal Subjects		− 8.4	−14.0	− 5.5		−20.7	−33.5	−13.8
Normal Subjects Induced Lipemia		−15.8	−14.7	—		−31.7	−26.4	—
Atherosclerotic Patients		− 9.5*	− 5.7	−13.0		−36.2*	−14.3	−24.7
Nephrotic Patients		− 7.2	− 8.8	−14.4		−12.8	−18.1	−24.8†

* Based on values for 4 patients.
† Based on neutral fat values of 6 patients.

mg. of heparin. In a third patient (J. G.), plasma clearing after 100 mg. of heparin was the same as with 50 mg., the fasting levels being quite similar. At a later date, with the plasma lipid somewhat lower (1,825 versus 2,375 mg. per 100 ml.), only slightly increased clearing followed a triple dose of 150 mg. of heparin.

Although the three main groups were too small to permit final conclusions, the determinations suggest that heparinized plasma of normal individuals cleared more rapidly than plasma of persons with coronary athero-

sclerosis, and that plasma of the nephrotic patients cleared even less. Differences in the behavior of plasma to heparin may well exist. Other workers have found that individuals vary in production of clearing factor.[5] It has also been reported that even in small doses heparin induced a lesser clearing in plasma of patients with atherosclerosis than in plasma of normal men, both groups having normal initial plasma lipids.[6, 7] It was inferred that

TABLE V

Plasma Lipid Partition before and after Heparin in Subjects with Idiopathic Lipemia (Group IV) (mg. per 100 ml.)

Patient	Mg. Heparin	Before Heparin	15 Minutes after Heparin	1 Hour after Heparin	2 Hours after Heparin
Total Lipids					
C. G.	10	895	735	695	705
S. Z.	25	1830	1570	1355	1285
M. M.	100	2090	1760	1210	1200
Cholesterol					
C. G.	10	192	189	196	184
S. Z.	25	206	213	197	192
M. M.	100	332	332	322	308
Esterified Cholesterol					
C. G.	10	129	124	136	119
S. Z.	25	137	136	128	131
M. M.	100	214	204	200	200
Phospholipids					
C. G.	10	209	209	216	203
S. Z.	25	322	368	280	260
M. M.	100	376	376	340	304
Neutral Fats					
C. G.	10	494	337	283	318
S. Z.	25	1302	989	878	833
M. M.	100	1382	1052	548	588
Per Cent Change in Total Lipids					
C. G.	10		−17.8	−22.3	−21.2
S. Z.	25		−14.2	−26.0	−29.8
M. M.	100		−15.8	−42.1	−42.6
Per Cent Change in Neutral Fats					
C. G.	10		−31.8	−42.7	−35.8
S. Z.	25		−24.0	−32.6	−36.0
M. M.	100		−23.9	−60.3	−57.5

there was a true relationship between atherosclerosis and the resistance of plasma to clearing by heparin, ascribed to abnormal inhibition or neutralization of heparin or to a basic abnormality in the state of plasma lipids, or to both factors.

Effect on Lipid Partition

The significant finding in the plasma lipid partition after heparin in all four groups was a decrease in plasma total lipid, due primarily to a fall in neutral fat (tables 4, 5). The extent of the fall in neutral fat was not related to its initial fasting level. Values for other lipids, namely, total cholesterol,

Table VI

Mean Plasma Cholesterol and Phospholipid before and after Heparin (Groups I, IA, II, III) (mg. per 100 ml.)

	Normals	Normals with Induced Lipemia	Coronary Atherosclerosis	Nephrosis
Total Cholesterol				
Fasting	176.6	189.6	257.4	597.7
15 minutes after heparin	183.0	190.6	259.4	612.0
60 minutes after heparin	182.4	188.0	254.4	587.1
120 minutes after heparin	178.0	—	244.2	588.4
Esterified Cholesterol				
Fasting	131.6	140.6	194.4	428.6
15 minutes after heparin	140.6	142.4	194.0	437.0
60 minutes after heparin	134.3	139.0	195.6	420.7
120 minutes after heparin	135.6	—	184.8	424.9
Phospholipids				
Fasting	213.0	247.6	267.4	429.3
15 minutes after heparin	212.8	256.0	259.8	450.1
60 minutes after heparin	213.8	251.6	273.8	439.0
120 minutes after heparin	216.2	—	257.0	386.2

esterified cholesterol and phospholipid, were surprisingly constant (table 6). Apparently heparin had no effect on these fractions throughout the two hour period of observation. Minor changes found were all within limits of experimental error and statistically insignificant.

Change in Neutral Fat

Normal Subjects (Group I): In four of the five fasting normal subjects an appreciable fall in neutral fats was observed. The mean figures before heparin, and 15, 60 and 120 minutes later were, respectively, 315.4, 250.2, 209.8 and 271.8 mg. per 100 ml. In percentage of the fasting level of

neutral fat, the fall was 20.7, 33.5 and 13.8 for the three post-heparin periods. A decline in neutral fat values was also observed in five normal subjects with induced lipemia (Group IA). Fifteen minutes and one hour after heparin there was an average change from 283.2 to 193.4 and 208.4 mg. per 100 ml., respectively. The fall after 15 minutes was 31.7 per cent, an amount larger than one would ascribe in such a short time to physiologic mechanisms of clearing at this stage of intestinal absorption. After one hour the fall was 26.4 per cent.

Atherosclerosis (Group II): The plasma of patients in this group also showed a decline in values for neutral fat after heparin. The mean fasting level was 386.2 mg. per 100 ml., which was moderately higher than that of the normals. The means obtained 15, 60 and 120 minutes after heparin were 246.3, 330.8 and 290.8 mg. per 100 ml., respectively. The fall from the original fasting level in the first 15 minutes was 36.2 per cent, after one hour 14.3 per cent, and after two hours 24.7 per cent. Four of the five patients in this group had a drop of at least 30 per cent in neutral fat at some time during the two hour observation period.

Nephrosis (Group III): Of the nephrotic patients in all but one (P. Z.) there was a decrease in plasma neutral fat after heparin. In another experiment, however, this patient did show the typical fall in neutral fat after a quadruple dose of 100 mg. of heparin. The mean neutral fat content of the fasting plasma for the group was 838.2 mg. per 100 ml., an abnormally high value. The post-heparin figures after 15, 60 and 120 minutes were 778.6, 737.7 and 630.5 mg. per 100 ml. In one of the nephrotic patients the fasting figure for neutral fat is missing, so that the percentage fall in neutral fat in table 4 is based on the means of six of the seven individuals. The mean change in neutral fat after heparin in this group was 12.8, 18.1 and 24.8 per cent after 15, 60 and 120 minutes.

Idiopathic Lipemia (Group IV): After receiving heparin, these patients presented a most striking fall in total lipid, particularly in neutral fat. As in the other three groups—normal, atherosclerotic and nephrotic—the values for plasma cholesterol, esterified cholesterol and phospholipids remained practically unchanged after heparin (table 5). The three subjects in this group had unusually high initial total lipid levels. The neutral fat of the child fell from 494 to 337, 283 and 318 mg. per 100 ml. at the 15, 60 and 120 minute periods, a decline of 31.8, 42.7 and 35.8 per cent. Similarly, the hyperlipemic gouty patient after 25 mg. of heparin exhibited a fall in neutral fat from 1,302 to 989,878 and 833 mg. per 100 ml., equivalent to a drop of 24, 32.6 and 36 per cent at the three post-heparin test intervals. Patient M. M. received 100 mg. of heparin, following which his initial neutral fat of 1,382 mg. per 100 ml. fell after 15, 60 and 120 minutes to 1,052, 548 and 588 mg. per 100 ml., representing percentage falls of 23.9, 60.3 and 57.5, respectively.

Although the effect of heparin in both normal and pathologic groups was characterized by a fall in neutral fat, the variations in extent and time of fall were considerable, resulting in large standard deviations of the means. On this account it was not possible to detect among the groups any contrasting pattern in behavior to heparin.

Effect of Increasing Dosages of Heparin: In three nephrotic patients we repeated the injection of heparin to determine a possible relation between dose and effect. Results of these comparative studies are given in table 7. As in the other tests, injection of heparin did result in a fall in neutral fat,

TABLE VII

Plasma Total Lipids and Neutral Fats after Varied Amounts of Heparin (Nephrotic Subjects) (mg. per cent)

Subject	Amount of Heparin	Before Heparin	15 Minutes after Heparin	1 Hour after Heparin	2 Hours after Heparin	Change after 15 Minutes		Change after 1 Hour		Change after 2 Hours	
						Mg.	%	Mg.	%	Mg.	%
Total Lipids											
R. McK.	15	1775	1580	1660	1420	−195	−11.0	−115	− 6.5	−355	−20.0
	35	2572	2315	2157	2042	−257	−10.0	−415	−16.2	−530	−20.6
P. Z.	25	1110	1190	1100	1140	+ 80	+ 7.2	− 10	− 0.9	+ 30	+ 2.7
	75	870	990	880	790	+120	+13.8	+ 10	+ 1.1	− 80	− 9.2
	100	890	840	800	750	− 50	− 5.6	− 90	−10.1	−140	−15.7
J. G.	50	2220	2135	2085	1875	− 85	− 3.8	−135	− 6.1	−345	−15.5
	100	2375	1905	1935	1735	−470	−19.8	−440	−18.5	−640	−26.9
	150	1825	1575	1445	1325	−250	−13.7	−380	−20.8	−500	−27.4
Neutral Fats											
R. McK.	15	809	600	665	494	−209	−25.8	−144	−17.8	−315	−38.9
	35	1226	953	811	804	−273	−22.3	−415	−33.8	−422	−34.4
P. Z.	25	505	605	518	558	+100	+19.8	+ 13	+ 2.6	+ 53	+10.5
	75	385	510	385	346	+125	+32.5	0	0	− 39	−10.1
	100	439	379	339	312	− 60	−13.7	−100	−22.8	−127	−28.9
J. G.	50	1608	1516	1403	1238	− 92	− 5.7	−205	−12.7	−370	−23.0
	100	1744	1334	1336	1182	−410	−23.5	−408	−23.4	−562	−32.2
	150	1266	1044	899	—	−222	−17.5	−367	−29.0	—	—

which, 15 minutes after the injection, seemed unrelated to the size of dose administered. At the end of one and two hours, however, the larger doses were associated with a greater depression in plasma neutral fat. An increase in dose of heparin did not effect any change in plasma cholesterol or phospholipid values.

DISCUSSION

The salient findings after heparin injection were a uniform depression of plasma neutral fat content in the normal as well as in the three pathologic

groups of individuals, together with plasma clearing of varying degree. In normal individuals given heparin during lipemia, the diminished lactescence of plasma appeared to be related to decrease in plasma neutral fat. On the other hand, in patients with hyperlipemia, extensive fall in plasma neutral fat did not go hand in hand with diminished lactescence. In a patient with idiopathic hyperlipemia with markedly opaque plasma (M. M.), there was no clearing despite a loss of over 50 per cent of its neutral fat. In a nephrotic patient with lipemic plasma (J. G.), there was similarly no change in its light transmission one hour after heparin, although neutral fat fell 29 per cent. In another patient with nephrosis (P. Z.), whose fasting plasma was originally translucent, there was no change in light transmission despite a fall in one hour of 22.8 per cent neutral fat. In another nephrotic patient with clear plasma (R. K.), its light transmission two hours after heparin was unaltered even though the plasma neutral fat content fell by 48 per cent. As mentioned above, light transmission through plasma is not determined solely by its lipid content. Other factors such as size of suspended particles and plasma proteins of the serum are known also to play a part in light transmission. Obviously, loss of neutral fat in plasma does not alone explain heparin clearing.

Other investigators have also found that clearing of plasma by heparin was accompanied by a fall in neutral fat with unchanged values for cholesterol and phospholipid.[5, 8] In a report of the effect of heparin in a patient with relapsing pancreatitis and essential hyperlipemia, an appreciable decrease in serum fatty acid occurred while cholesterol and phospholipid content remained unaltered.[9] One group of workers believed that a fall in serum cholesterol followed the use of therapeutic doses of heparin in patients with nephrosis and myocardial infarction.[10] In the present study, single doses of 100 and 150 mg. of heparin did not produce any significant reduction in plasma cholesterol during an observation period of 15 to 120 minutes.

Comment on Action of Heparin

There is no accepted understanding of how heparin effects the clearing of lipemic plasma, although several physical and chemical mechanisms have been suggested. To clarify present thought on the subject, a brief digest of major contributions in the recent literature is presented here.

The original demonstration that lipemia of dogs could be made to disappear soon after an injection of heparin was made only in vivo.[11] Subsequently, in vitro clearing was produced by adding cleared heparinized plasma to untreated lipemic plasma, indicating that in the animal organism heparin in some way is modified and activated.[12] Clearing of lipemic plasma could also be induced by heparin-like substances such as sulphonated polysaccharides and pontamine fast pink, B. L.[13] In a similar way the synthetic anticoagulants Treburon and Paritol can effect lipemic clearing.[14] It was

observed also that clustering of chylomicrons of lipemic plasma could be induced in vitro by large amounts of heparin.[15]

The site at which heparin is activated is not apparent. Although in early animal experiments no single organ was found responsible for the clearing action of heparin,[16] in later restricted perfusion studies in animals so-called clearing factor was obtained in appreciable amounts from the abdominal and thoracic regions, especially from the heart and lung tissue, whereas none was obtained from the hind limbs. A fairly stable preparation of clearing factor has been made from finely ground lyophilized rat pylorus.[17, 18] Other workers believed that a thromboplastic protein from the lungs combined with heparin with displacement of a phospholipid constituent and formation of a heparin-protein complex.[19] In studies of the effect of heparin on chylomicron counts through localized injections and blood sampling, it was found that in the legs and lungs of dogs an injection of heparin initiated prompt clearing of lipemia. This immediate response was not found in the capillaries of the brain.[20]

The action of heparin, attributed to a postulated antichylomicronemic factor, was found associated with a fall in plasma surface tension ascribed to formation of a surface-acting phospholipid complex.[12] Bearing on such a surface-active complex was the conclusion reached in studies of certain physicochemical properties of heparin in which its oxidizing effect on leukomethylene blue was measured. It was thought that heparin, with its high molecular weight and high negative charge, could adsorb on its surface the basic molecules of leukomethylene blue, thereby making them very sensitive to oxidative influences.[21]

In addition to changes in the plasma protein patterns found in dogs receiving heparin as shown by paper chromatography, a reduced sedimentation rate, a fall in hematocrit values and a reduction in chylomicron count have been reported.[22] It was suggested that the addition of heparin to blood results in an increased tendency of red blood cells and chylomicrons to cluster, and that these aggregates are filtered out by the capillaries, with consequent disappearance of chylomicrons from the plasma.[15] Dissolution of chylomicrons in dark field preparations of heparinized whole blood has also been observed. Since the chemical composition of chylomicrons was found to consist of 97 per cent neutral fat and 3 per cent cholesterol, it was concluded that clearing of plasma by heparin was accompanied by a shift of neutral fat from a visible to an invisible or dissolved state.[23]

In studies using the ultracentrifuge, alteration of the lipoprotein spectrum has been observed after heparin in animals and man characterized by rapid conversion of large lipoprotein molecules into small ones. Alteration of the lipoprotein pattern with heparin could not be produced in vitro. However, when heparinized plasma was added to non-heparinized serum, lipoprotein molecules were altered in the direction described above. This presumably "active principle" produced by heparin was found to reside in the globulin fraction.[24]

Confirmation of the latter finding was reported by other workers who fractionated plasma and made in vitro assays of precursors of the heparin clearing factor. Perfusion experiments indicated that a plasma constituent in the presence of heparin was converted into clearing factor by a tissue catalyst. From centrifuged lipemic dog plasma a lipoprotein substrate was prepared to which purified clearing factor was added. Anticipated clearing did not occur unless some infranatant plasma was also added, suggesting involvement of a co-protein in the clearing system. It was concluded that in vivo administration of heparin leads to the production of the "clearing factor," which in the presence of a second plasma protein, a "co-protein," brought about the observed changes in plasma turbidity and flotation rates. With active clearing a reorientation of lipoproteins was observed, consisting of a decrease in the ultracentrifugal flotation rates of low density lipoproteins and a concomitant production of alpha lipoprotein molecules.[17, 18] In electrophoretic as well as paper-electrophoretic studies, increase in alpha-lipoprotein and appearance of a new peak between the albumin and alpha-globulin fractions were found associated with heparin clearing.[26, 27]

Finally, in exploring the interaction of heparin active factor and lipoproteins, fatty acid was found to be liberated, presumably through a lipolytic mechanism. Turbidity which usually developed after incubating normal serum with a solution of egg-yolk lipoprotein failed to develop when normal serum was replaced by plasma from a heparinized individual. This suppression of the development of turbidity in egg protein solution occurred only after heparin active factor had been previously incubated with lipid. When heparin active factor was incubated with egg-yolk lipoprotein, titratable fatty acid was liberated. It was also found that sodium oleate by itself could directly prevent development of turbidity in egg lipoprotein solution.[25]

At present it is not possible to formulate a picture of the complete mechanism of heparin action. It is probable that heparin, an anticoagulant, operates in the body in a complicated milieu, analogous to that which exists in the case of thrombin, a coagulant factor, which requires a combination and interaction of specific substance, cells, enzymes and minerals. Consequent to the injection of heparin the observed dissolution of chylomicrons, composed largely of neutral fat, explains in part the phenomena of the clearing of lipemic plasma, the change in neutral fat content and the liberation of fatty acid. It may well be that fragmentation of plasma-borne fat particles into smaller units and their dissolution by heparin are devices to facilitate the transit of dissolved neutral fat through the capillary cell wall.

The difference in the clearing of plasma in normal and certain pathologic states emphasized in the present investigation may be related in the latter to inhibition of heparin action. The relative persistence of plasma opacity after heparin, despite loss of neutral fat, in nephrosis and especially in idiopathic hyperlipemia suggests the existence in these conditions of other physical or chemical abnormalities, the nature of which remains to be demonstrated.

Summary

A comparison was made of the effect of intravenously injected heparin on plasma lipid partition and plasma clearing in 25 individuals consisting of 10 normal men, five patients with atherosclerosis recovering from recent myocardial infarction, seven patients in the nephrotic state of nephritis and three with idiopathic hyperlipemia.

Blood samples drawn before heparin administration and 15, 60 and 120 minutes later indicated an appreciable reduction in plasma total lipids, primarily in neutral fat content. Plasma cholesterol, esterified cholesterol and phospholipid fractions were unaffected.

In five normal subjects with a mean fasting plasma neutral fat content of 315.4 mg. per 100 ml., after 15 minutes neutral fat was reduced by 20.7 per cent and after 60 minutes by 33.5 per cent. In five normal individuals with induced alimentary lipemia and initial mean plasma neutral fat level of 283.2 mg. per 100 ml., there was a drop of 31.7 per cent in this constituent 15 minutes after heparin, an amount larger than one would attribute to physiologic fat clearance in this brief interval.

In five patients with coronary atherosclerosis whose mean fasting plasma neutral fat level was 386.2 mg. per 100 ml., heparin injection was followed by a fall in neutral fat of 36.2, 14.3 and 24.7 per cent after 15, 60 and 120 minutes, respectively.

A group of patients with nephrosis with a high mean fasting plasma neutral fat content of 838.2 mg. per 100 ml. showed an appreciable reduction in neutral fat after heparin. There was a fall of 12.8, 18.1 and 24.8 per cent after 15, 60 and 120 minutes, respectively. In this group an increase in size of dose of heparin from 15 to 35 mg. in a child and from 25 to 100 mg. in one adult and from 50 to 150 mg. in a second adult effected a somewhat greater reduction in plasma neutral fat content.

In three patients with idiopathic hyperlipemia with high plasma total lipids up to 2,090 mg. per 100 ml., varied doses of heparin effected a large and rapid reduction in neutral fat. In this group the per cent fall in neutral fat within a two hour period after heparin ranged from 23.9 to 60.3 per cent.

As measured by light transmission, plasma opacity or turbidity was reduced after heparin injection in all groups but to a variable extent. Plasma of normal subjects, and especially that of normal men with induced alimentary lipemia, cleared to a greater degree than plasma of patients in the other three categories. Fasting plasma of patients with nephrosis and essential hyperlipemia, usually opaque before heparin injection, cleared least of all. In the nephrotic group an increase in dosage of heparin did not affect plasma lactescence. As mentioned above, the technical difficulty of discovering changes in transparency in markedly opaque plasma must not be overlooked.

Light transmission of plasma was associated only in a general way with its lipid content. In patients with nephrosis and essential hyperlipemia,

plasma clearing induced by heparin seemed unrelated to the observed fall in neutral fat.

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ERYTHROPHAGOCYTOSIS AND HEMOSIDEROSIS IN LYMPH NODES, SPLEEN AND LIVER IN PATIENTS DYING OF MALIGNANT HYPERTENSION, CHRONIC GLOMERULONEPHRITIS AND PYELONEPHRITIS AND POLYCYSTIC DISEASE *

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The occurrence of erythrophagocytosis and hemosiderosis in reticuloendothelial structures in association with the anemia of uremia of experimental animals [1, 2, 3] suggested the need to determine whether such alterations occur in human tissues in association with bilateral renal disease causing renal failure and anemia. Such a study is reported below.

Selection of Cases

Twenty-eight cases of uremia without selection were studied. Abdominal and thoracic lymph nodes, spleen and liver were examined microscopically after staining with hematoxylin and eosin and iron stains. The morphologic changes in lymph nodes, spleen and liver searched for included hemorrhages in the peripheral and medullary sinuses of lymph nodes and erythrophagocytosis and hemosiderosis of all structures. The hemosiderosis of the liver recorded was confined to the Kupffer's cells, since no attempt was made to identify specifically the pigments within parenchymal cells. The results of the morphologic observations were then correlated with the type of renal disease as determined by the microscopic study of the kidneys, the degree of azotemia and the level of red blood cell count and hemoglobin concentration of the blood.

With one exception, all patients were males of ages varying between 22 and 60 years (average, 45 ± 14). All patients had hypertension, azotemia and abnormal urinary findings. The hypertension for the entire group varied between 170/100 and 250/160 mm. of Hg (mean systolic, 220 ± 28; mean diastolic, 139 ± 17). The blood urea nitrogen concentration varied between 21 and 294 mg. per 100 c.c. (average, 135 ± 64). Proteinuria, cylindruria and evidence of depressed excretory renal function (low specific gravity, depressed phenolsulfonphthalein or urea clearance) were demon-

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TABLE I

Summary of the Findings in Lymph Nodes, Spleen and Liver

	Malignant Hypertension		Glomerulo-nephritis		Pyelonephritis Cystic Disease		Total	
	Number Cases*	Anemic Cases	Number Cases	Anemic Cases	Number Cases	Anemic Cases	Number Cases	Anemic Cases
Lymph Nodes	11	8	6	5	2	2	19	15
Hemorrhages in	5	4	3	2	2	2	10	8
Erythrophagocytosis in	6	5	3	3	2	2	11	10
Hemosiderosis in	5	4	4	3	2	2	11	9
Spleen	15	10	8	7	4	4	27	21
Erythrophagocytosis in	3	3	2	2	0	0	5	5
Hemosiderosis in	7	7	5	4	1	1	13	12
Liver	15	9	8	7	4	4	27	20
Hemosiderosis in	9	8	6	5	4	4	19	17

* By "number cases" is meant the number of cases in each category for which specimens of lymph nodes or spleens or livers were available for study. These cases are further subdivided into those that displayed anemia.

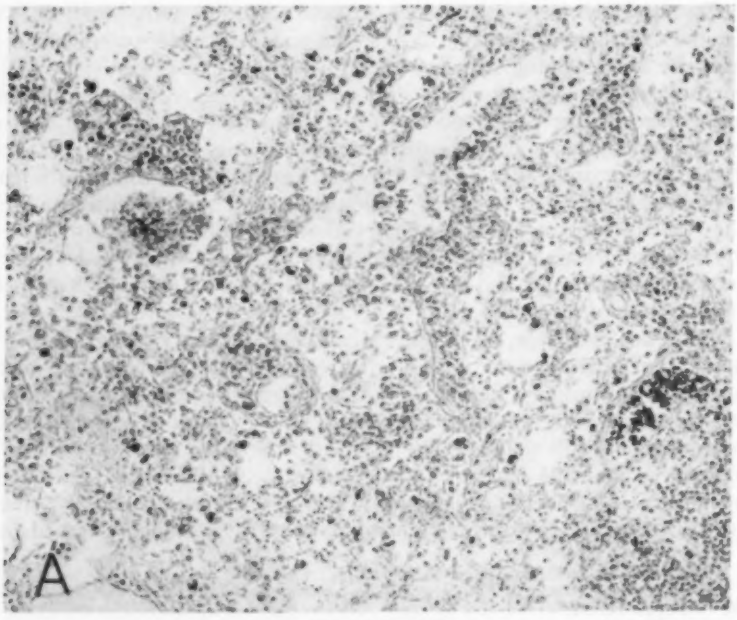


FIG. 1. *A.* × 150. Iron stain. Abdominal lymph node demonstrating erythrocytes in lymph sinuses and hemosiderosis. (The dark spots represent hemosiderin.) (White male, age 60, malignant hypertension; BP, 240/120; blood urea, 157 mg. per 100 c.c.; hemoglobin, 10 gm. per 100 c.c.; received no transfusions.)

strated in every case. All patients with malignant hypertension and glomerulonephritis exhibited microscopic hematuria. Considering anemia to be present when the hemoglobin concentration was 11.5 gm. per 100 c.c. of blood or less, we found 80 per cent of the patients to be anemic. The hemoglobin concentration of the anemic group varied between 6 and 11 gm. per 100 c.c. (average, 9.5 ± 1).

Results

The morphologic findings are summarized in table 1. Of 16 examples of malignant hypertension, 10 exhibited the triad of hypertension, renal insufficiency and anemia as defined above. All 10 revealed erythrophago-

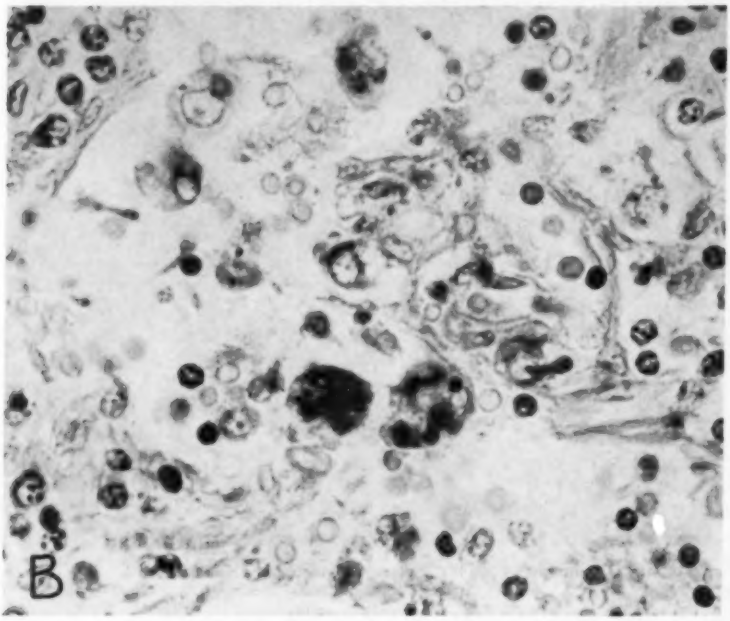


Fig. 1. *B*. Same as *A* × 840. Macrophages in lymph sinus containing intact and degraded erythrocytes and hemosiderin granules.

cytosis and/or hemosiderosis within at least one reticuloendothelial structure, and eight revealed these changes in two or more RE structures. (See figure 1.) Seven of eight patients with chronic glomerulonephritis had hypertension, renal failure and anemia. All but one of these revealed the changes in RE structures. All examples of chronic pyelonephritis and cystic disease revealed hypertension, renal failure, anemia and the changes in the RE structures.

In table 1 the incidence of the morphologic alterations within the RE structures is subdivided into that in all cases as well as that in the anemic group only. The changes in the RE structures occurred in the non-anemic group as well, and as such appeared to be either a fundamental component of the uremic state or a common complication of it. However, the data in table 1 suggest that the morphologic changes in the RE structures are more prone to occur in chronic renal disease with uremia and hypertension when anemia is also present. Thus, hemosiderosis of lymph nodes was encount-

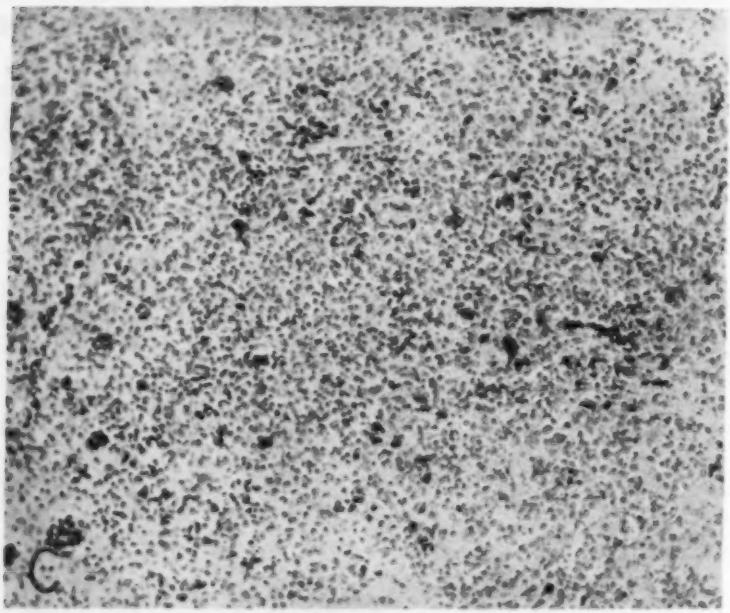


FIG. 1. *C*. Same as *A* × 145. Spleen demonstrating hemosiderosis. The dark granules represent hemosiderin.

ered in a total of 11 of 19 cases, but of these 11 cases, nine were in the anemic group; hemosiderosis was encountered in 13 of 27 spleens studied, and of these 13 cases, 12 were in the anemic group; and finally, hemosiderosis was observed in 19 of 27 livers, and of these 19 cases, 17 were in the anemic category. Twenty-one of 27 patients revealed anemia, and only one of these 21 failed to reveal changes in the RE structures, and in this one case lymph nodes were not available for study. Of the seven non-anemic subjects (hemoglobin, 12.9 to 17.8 gm. per 100 c.c. blood), three showed changes in the RE structures.

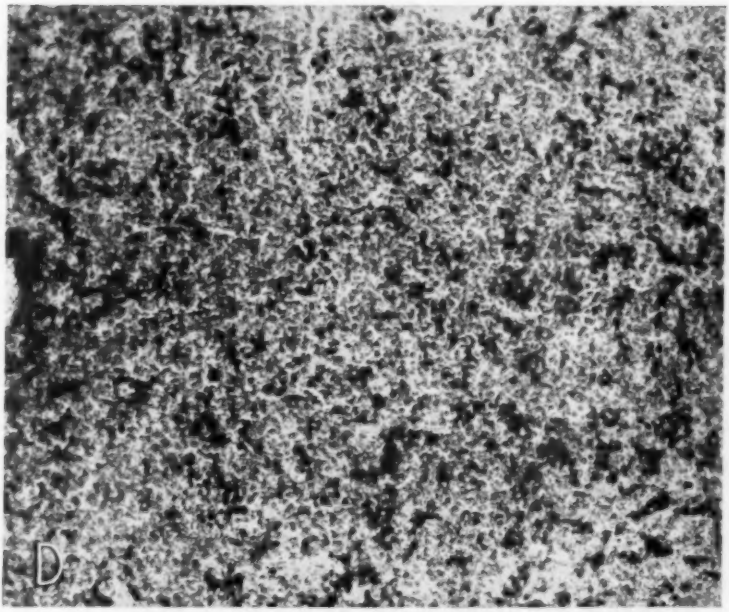


FIG. 1. *D.* (White male, age 31, subacute glomerulonephritis, BP 160/90; blood urea, 472 mg. per 100 c.c.; hemoglobin, 8.5 gm. per 100 c.c.; had received 5 blood transfusions, 500 c.c. each.) Iron stain. Spleen showing marked hemosiderosis.

COMMENT

Hemosiderosis of the spleen and liver occurs mainly as a result of an excessive exogenous intake of iron, as through the intestine or by blood transfusions,[4, 5] or as a consequence of a breakdown of red blood cells, usually attended by a continued intake and absorption of iron via the intestines.[6] In hemolytic states the iron deposits are particularly prone to involve the splenic pulp and the Kupffer's cells of the liver.[7] In most of the cases herein considered transfusional hemosiderosis was ruled out, since most of these patients did not receive blood. Consequently, the two possible sources for the iron were (1) solely enterogenous, or (2) due to a combination of a breakdown of red blood cells and continued intestinal absorption of iron. The present study does not elucidate either of these mechanisms. The morphologic changes within reticuloendothelial structures in human uremia herein described were formerly noted in experimental uremia [1, 2, 3] in which a hemolytic anemia was identified. Whether these morphologic changes (erythrophagocytosis and hemosiderosis) in man are related to the pathogenesis of the anemia as encountered experimentally remains to be demonstrated.

Summary

Morphologic changes within reticuloendothelial structures (hemorrhages, erythrophagocytosis and hemosiderosis of lymph nodes, erythrophagocytosis and hemosiderosis of the spleen, and hemosiderosis of the liver) have been observed in 20 of 21 cases of advanced bilateral renal disease associated with the clinical triad of hypertension, renal insufficiency and anemia. Similar findings were noted in three of seven non-anemic cases. These findings are similar to those previously described in experimental uremia associated with a hemolytic anemia. It is suggested that in some instances these changes may be related to the pathogenesis of the anemia of uremia in man.

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UNUSUAL ETIOLOGIES OF PORTAL SYSTEM HYPERTENSION (TORULOSIS, PHLEBOSCLEROSIS AND RETROPERITONEAL CHRONIC INFLAMMATION) *

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Interest in the problem of portal hypertension has been renewed since successful new operative procedures have been devised to relieve the increased pressure in the portal system.[1, 2, 3, 4, 5] The recognition of this syndrome presents no major problem, particularly if a stage is reached in which pronounced signs and symptoms are present. These consist of a history of hematemesis and/or melena, the presence of ascites, splenomegaly and enlarged collateral veins in the abdominal wall, and x-ray evidence of esophageal varices. The anatomic basis for this condition has been described [6] the experimental work on this subject reviewed,[7, 8] and some of the clinical problems have been discussed.[9]

The etiology of each case of portal hypertension may present great diagnostic difficulties. The majority of the cases are caused by intrahepatic obstruction of the portal circulation, notably in cirrhosis of the liver. Extensive experience has been gathered in this disease and numerous diagnostic procedures are available.[10] In a smaller number of cases of portal hypertension, obstruction of the portal blood flow is caused by disease processes located outside of the liver. These may be classified as arising from structures adjacent to the portal tree, and consist of lymphomas and neoplasms,[11, 12] inflammation [13] or granulomas,[14] leading to narrowing of the portal vein, and thrombosis. The process may arise in the venous wall itself, as in pylephlebitis, syphilitic and tuberculous phlebitis, or phlebosclerosis,[15, 16, 17] or it may be congenital.[3]

Finally, portal vein obstruction may be caused by so-called spontaneous thrombosis such as is encountered in blood dyscrasias, most commonly in polycythemia vera.[18] The site of the primary obstruction may be the hepatic vein as well as the portal vein.[9] Portal hypertension due to extrahepatic obstruction presents much greater differential diagnostic difficulties than that due to intrahepatic causes. Recognition of the etiologic factor is of the utmost importance, because the possibility of successful surgical intervention and the future course of the disease in patients who have had successful shunt operations will depend upon the basic causative process.

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The purpose of this paper is to report three cases of portal hypertension occurring under unusual circumstances, of interest because of the rare etiology.

Case Reports

Case 1. A 30 year old white salesman was admitted to The Chicago Memorial Hospital in November, 1951, with complaints of breathlessness, weakness, poor appetite and pain in abdomen and legs. Hematemesis had occurred three days before admission and the subsequent stools were black. The present illness had started in 1949 with swelling in the ankles, which rapidly progressed so that the patient was unable to walk. The urinary output was decreased at that time. In 1950 an enlarged liver and jaundice were found on physical examination. At that time the patient started vomiting repeatedly, and he believed that he had fever. He remained chronically weak and ill. The stools were never clay-colored, but the urine was often scanty and dark. The patient stated that this first episode of jaundice subsided after several weeks and reappeared a few weeks later. In October, 1951, he had vomited blood for the first time and since then had had repeated hematemesis. He was admitted to another hospital, where the diagnosis of liver cirrhosis was made. Several peritoneal taps were performed and he received blood transfusions. Subconjunctival ecchymoses developed in October, 1951. At that time he also coughed heavily and expectorated bloody sputum.

During World War II he had been in North Africa, Italy and France, where he suffered a face injury which required grafting of skin. There was no history of hepatitis or jaundice during his period in the service. The patient had never been seriously ill before. He had been drinking considerable amounts of beer. After the war years he settled in the midwestern United States and never left this location.

On examination the patient appeared acutely and chronically ill and showed signs of considerable weight loss. At times he was confused. The pulse and respirations were rapid; the blood pressure was 150/80 mm. of Hg. The temperature on admission was 104° F. Extensive subconjunctival ecchymoses involving the scleral and palpebral portions were present. The eye grounds were normal. Slight jaundice was noticed. A 4 plus pitting edema was present over the legs and the sacral region. Small but hard discrete lymph nodes were felt in the cervical and axillary regions. On percussion of the chest both diaphragms were high and moved slightly with respiration. Dullness was present over both lower lobes, and showers of moist râles were heard bilaterally. The heart was not enlarged. A grade 1–2 systolic murmur was heard over the apex. The abdominal cavity contained considerable ascitic fluid. The liver was felt 7 cm. below the costal margin, and was smooth, hard and nontender. The spleen was enlarged and firm, and could be felt 3 cm. under the costal arch. No abnormal masses were felt on rectal examination. The neurologic examination was negative, and there was no nuchal rigidity and no Kernig's sign. An x-ray of the chest showed elevation of the diaphragms, pleural thickening in both costophrenic angles and in the right interlobar region, and adhesions about the right diaphragm. The urine had a specific gravity of 1.011, and contained no albumin or sugar. Microscopically, several finely granular and occasional cellular casts were present. The hemoglobin was 6.1 gm.; red blood cells, 1,930,000; white blood cells, 12,950; hematocrit, 21 per cent. There were 82 segmented polymorphonuclears, 1 eosinophil leukocyte, 3 myelocytes, 4 monocytes, and 10 lymphocytes per 100 cells. Some spherocytes and target cells were seen. The platelet count was 156,000; the prothrombin time was 24 sec. The fasting blood sugar was 110 mg. per cent; the blood urea nitrogen, 17.2 mg. per cent. Total serum protein was 6.5 gm. per cent, with 2.1 per cent albumin and 4.5 per cent globulin. The serum bilirubin was 6.4 mg.

per cent; total cholesterol, 146 mg. per cent, with 46 per cent esters. Thymol turbidity was 3.9 units. Cephalin flocculation test was 4 plus. Kahn test was negative. The serum alkaline phosphatase was 9.8 units. Blood cultures were negative, and stool cultures showed no pathogenic organisms. Spinal fluid was clear, with a total protein of 38 mg. per cent, and there were no cells.

The diagnosis of hepatic cirrhosis was first entertained, but in view of the high fever and the generalized lymphadenopathy it was felt that the patient had a lymphoma, possibly Hodgkin's disease. Biopsy of a cervical lymph gland was performed and revealed a granulomatous lesion containing large numbers of *Cryptococcus neoformans* (Torula). Cultures of the peritoneal fluid yielded the same organism. The patient's course was characterized by high fever and chills, several spells of hematemesis and melena, and increasing jaundice. Several abdominal paracenteses were performed. The patient received a number of blood transfusions and was treated with sulfadiazine, potassium iodide and penicillin. He died on the eighteenth hospital day shortly after a convulsive episode.

The postmortem examination revealed the following significant changes: The skin was intensely jaundiced. The peritoneal cavity contained about 2,000 c.c. of a slightly turbid amber fluid. The mediastinal and mesenteric lymph nodes were enlarged, measuring 3 cm. in greatest diameter. They were soft and confluent, and contained a purulent green material. In the abdomen such nodes were located in the region of the porta hepatis surrounding the cystic and common bile ducts. Irregularly distributed throughout the lungs were numerous firm, yellowish gray nodules measuring 1.5 cm. The liver weighed 1,700 gm. The surface was coarsely granular and there were flat scars. On section the normal architecture was distorted and there were brownish yellow nodules and irregular green areas. The extrahepatic bile ducts were patent. The portal vein was surrounded by large lymph nodes. There were no thrombi. The spleen weighed 530 gm., and was diffluent and hemorrhagic. Varices were seen in the lower portion of the esophagus. Permission to examine the brain was not granted.

Microscopic examination of the organs revealed granulomas in the lungs and lymph nodes. In the lungs the granulomas were small, well demarcated and surrounded by concentrically arranged fibrous tissue. Within the center there were a granular fibrillar acidophilic material and multinucleated giant cells. The *Cryptococcus neoformans* organisms were found either in the giant cells or lying free in the tissue (figure 1). External to this were many epithelioid cells, round cells, a few plasma cells and eosinophils, and rare granulocytes. In the lymph nodes the granulomas were larger, with little or no surrounding fibrosis. There were many organisms. The epithelioid cells assumed a pallisade arrangement.

The liver was the seat of a postnecrotic cirrhosis. The capsule was thickened by an increased amount of dense fibrous tissue. There were nodular elevations which were composed of regenerated liver cells. Many small bile ducts were proliferating and appeared to be in the process of forming liver cells. These were embedded in a large amount of young connective tissue which contained a moderate number of round cells. The orderly hepatic architecture was replaced by fairly uniform nodules of regenerated liver cells, surrounded by thick bands of fibrous tissue which enclosed the nodules and anastomosed with each other. The central veins were displaced to the periphery of the lobule or were not evident. The hepatic cells were large, with nuclei of variable size, and a finely granular or vacuolated cytoplasm. Some contained bile pigment. Many of the cells, especially at the periphery of the lobule, contained two nuclei. Within the bile canaliculi were bile thrombi. The radicles of the portal veins were distended with blood (figure 2). In the spleen there were large numbers of granulocytes in the pulp. Some of the veins were filled with thrombi. The sinusoids were engorged with blood; there were many hemorrhages and one large infarct.



FIG. 1. *Case 1. Cryptococcus neoformans* in lymph node (× 900). The dense capsule of the organism is prominent. Periodic acid—Schiff's stain.

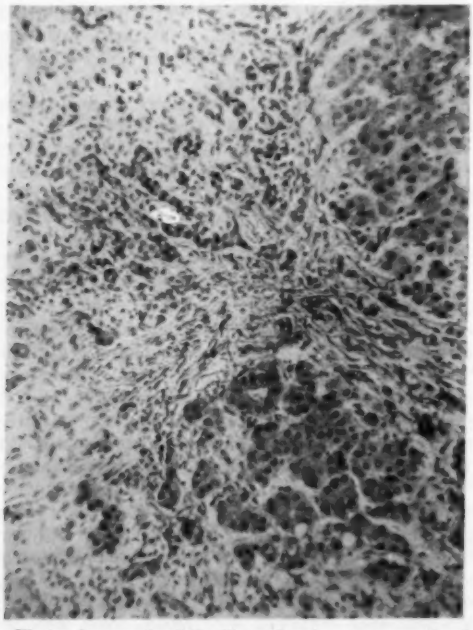


FIG. 2. *Case 1.* Photomicrograph of the liver showing postnecrotic cirrhosis (× 140). Iron hematoxylin stain.

The *Cryptococcus neoformans* was identified by its typical appearance of round, double-wall refractile cells, some of them showing typical budding. Cultures of the biopsied gland and of the peritoneal fluid on Sabouraud's glucose-agar, Littman's ox gall and beef heart-agar with blood at 37° or 22° produced rapidly growing colonies which became mucoid within two or three days, turning from translucent to pink, and eventually to brick red. The organism utilized dextrose and saccharose, producing acid but no gas. No true spores appeared. Three mice inoculated intraperitoneally developed tumor-like formations, or smaller nodes in the peritoneal cavity with adhesions and patchy splenic lesions. The organism was recovered from some of these granulomas.

Comment: This patient presented himself with the clinical picture of portal hypertension, the cause of which proved to be partly an infestation of portal lymph nodes with *Cryptococcus neoformans* (Torula). The same organism was found in the lungs, the mediastinal lymph nodes and the peritoneal fluid. A severe toxic cirrhosis of the liver which was also present played a major part in the development of the syndrome. Compression of the common duct by the portal lymph nodes may have played a rôle in the production of jaundice.

Case 2. A 21 year old white female telephone operator presented herself because of tarry stools which appeared about 10 days prior to her hospital admission. She had then experienced several episodes of dizziness and sharp epigastric pain, unrelated to meals, mostly after bending over. These were frequently followed by the elimination of black stools. She had also noticed shortness of breath on exertion. She had been working regularly until about 10 days before entry to the hospital. When questioned by systems she denied having been seriously ill at any time. As a child she had had measles, chickenpox and mumps. In particular, there was never any illness suggesting abdominal involvement, either in infancy or later. The patient did not smoke or drink, and used no narcotics. Her menstrual history was not significant, and she was unmarried. Both parents were of German descent, and were living and well, as were her two brothers and four sisters. Her mother had not been sick during her pregnancy with the patient.

On examination the temperature was 99.4° F.; pulse, 82; respirations, 16; blood pressure, 112/68 mm. of Hg. The skin and the mucous membranes were pale. The patient was alert but looked acutely ill. There was no lymphadenopathy, no distended veins were seen, and no petechiae were present. The mouth was normal. The thyroid was not enlarged and no abnormal pulsations were observed. The lungs were normal on percussion and auscultation. The heart seemed not enlarged. There was a grade 1 systolic murmur over the apex, and the rhythm was regular. The abdomen was slightly protuberant, but no shifting flank dullness could be elicited. The liver edge was felt 6 cm. below the costal arch; its surface was smooth, its consistency hard. Tenderness was present in the right and midepigastrium. The spleen could be felt 4 cm. below the left costal arch. It was firm and not tender. No other masses or tenderness was found in the abdomen. The umbilicus was normal. Rectal examination was negative. The reflexes were normal and no pathologic reflexes could be elicited. The urine had a specific gravity of 1.015; it contained no sugar and no albumin; rare red cells and white cells were seen, but no casts. The hemoglobin was 8 gm.; red blood cells 3.59 million (1.5 per cent reticulocytes); white blood cells, 12,500, consisting of 81 per cent polymorphonuclears, 3 per cent eosinophils, 2 per cent basophil leukocytes, 12 per cent lymphocytes and 2 per cent monocytes. The Kahn

test was negative. The platelet count was 330,000, and the prothrombin time was 18 seconds. The bleeding and coagulation times were normal. Total serum protein was 6.1 gm./100 c.c.; albumin, 3.9; globulin, 2.2. The thymol turbidity and the flocculation were 1 plus; cephalin flocculation, 2 plus. Total cholesterol, 190 mg. per cent, with 66 per cent esters. The stool was negative for ameba and showed a positive benzidine test. A bone marrow specimen revealed a pattern compatible with recent hemorrhage. X-rays of the chest, gall-bladder, stomach, duodenum and colon were normal. On intravenous pyelography the right kidney appeared depressed by the large liver, but no other abnormalities were noted. Skin test for histoplasmosis was negative.

During the first seven days in the hospital the temperature rose occasionally to 101° rectally, but there was no noticeable change in the patient's complaints. On the eighth hospital day it was noticed that the abdomen was markedly protuberant, and a very definite shifting dullness appeared. Three days later three quarts of straw-colored clear fluid were removed from the abdominal cavity. This proved to be a transudate and yielded no bacteria on culture. A blood culture was also negative. The diagnosis of liver cirrhosis with portal vein thrombosis was maintained, but in view of the sudden appearance of ascites and the rapid progression of the disease it was feared that the patient might have a neoplasm and an exploratory operation was decided upon. On the sixteenth hospital day a laparotomy was performed. Under local anesthesia a right rectus incision was made. On opening of the peritoneal cavity a large amount of ascitic fluid was aspirated. The midportion of the edge of the right lobe of the liver was found to be the site of a bulbous enlargement, the appearance of which suggested hemangioma. A needle puncture was made into this apparent tumor and blood was freely aspirated. The bleeding from the puncture was controlled with Gelfoam. Pressure of one of the veins in the gastrocolic ligament was measured with a water manometer and found to be 350 mm. of water. The abdomen was closed in layers and the patient's condition remained unchanged by this procedure. The patient passed large tarry stools postoperatively, and it was decided to perform a venous shunt operation. On the twentieth postoperative day, under cyclopropane-ethylene intratracheal anesthesia through combined thoraco-abdominal approach, the site of the spleen was exposed. It became apparent that a thrombosis of the splenic vein and numerous other splanchnic vessels existed. The patient's condition was extremely poor and a splenectomy was performed quickly. The patient died on the operating table immediately following this procedure.

At the postmortem examination the pertinent findings were as follows: The liver weighed 2,370 gm. The capsule was focally opaque. The surface, especially of the right lobe, was wrinkled, and there were small, irregular, elevated yellow nodules. The consistency was soft and flabby. On section it appeared that only the peripheral 4 to 7 cm. resembled normal liver tissue. The main mass of the liver was yellowish brown and bulging. Structurally it resembled liver, but the cords were thicker and coarser. There were focal hemorrhages and soft areas at the periphery. The caudate lobe was only partially involved. The portal vein radicles were filled with recent thrombi. The main hepatic veins were narrowed and a probe could not be passed beyond a distance of 5 cm. from the confluence of the main hepatic vein with the inferior vena cava. The intima of the hepatic veins and of the inferior vena cava was thickened, and in the latter there was a recent thrombus. The spleen (removed at the time of surgical exploration) weighed 614 gm. It was firm, brick red and glassy. The splenic and superior mesenteric veins contained recent thrombi.

Microscopic Description: Sections of the liver taken from the subcapsular areas revealed a large amount of periportal fibrosis with an infiltration of round cells and rare plasma cells. There was an increased number of small bile ducts. Fusion of the fibrous tissue had taken place with an isolation of islands of hepatic cells. The

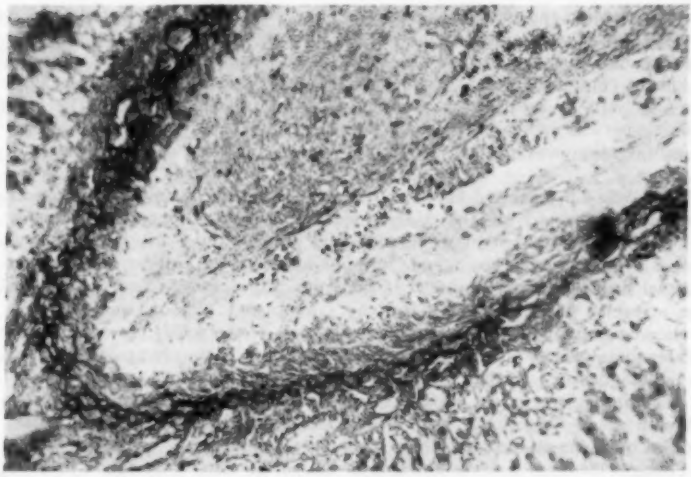


FIG. 3. *Case 2.* Radicle of portal vein (× 140). The venous wall is thickened and the lumen filled by a thrombus. Orcein stain.

central veins were absent or eccentric in position; they were dilated, and there was an increased amount of fibrous tissue surrounding them. The large and small radicles of the portal vein were partly or completely filled with recent and organizing thrombi (figure 3). Sections of the main mass of liver tissue revealed large, irregular cords separated by dilated sinusoids. Some of the bile capillaries were filled with bile thrombi. The hepatic veins were never centrally placed but were either eccentric

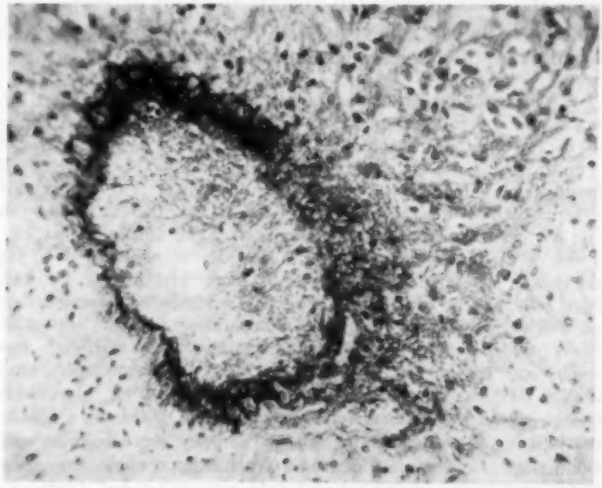


FIG. 4. *Case 2.* Hepatic vein (× 280). Note considerable thickening of venous wall and thrombosis. Orcein stain.

or incorporated in the periportal spaces. They were small, the walls thick and the lumens narrowed. At times there was no apparent lumen. The intima often comprised one-half the thickness of the wall and was composed of loose fibrous tissue. The lumens contained recent, organizing and organized thrombi with recanalization (figure 4). In areas there were early infarcts or hemorrhages. The periportal fibrous tissue was increased in amount, with fusion of adjacent portal areas. Bile duct proliferation was present, but there was no evidence of regeneration of liver cells.

There was a pronounced fibrosis of the pulp of the spleen, with proliferation of the sinusoids and atrophy of the Malpighian corpuscles. Pronounced changes of a varying degree were seen in the hepatic and portal veins. The subintima was the broadest layer, and often comprised from one-half to three fourths of the thickness of the vessel walls. It was composed of concentrically arranged and loosely laminated tissue. Special stains, including the van Gieson and Masson, and Gomori's stain for reticulum, revealed that the predominant tissue of the subintima was collagen with small numbers of smooth muscle and elastic fibers. These changes were compatible with the diagnosis of phlebosclerosis.

In addition, some of the hepatic veins were dilated and in many the lumens were filled with recent, organizing and recanalized thrombi. However, the portal veins contained only recent and partially organizing thrombi.

Changes identical with those found in the portal veins were found in the splenic, superior and inferior mesenteric veins.

Other veins of the body were free of changes. In some of the pulmonary and coronary veins there were small masses of fibrin.

Comment: A young woman with a short clinical history developed melena and suddenly appearing ascites. The underlying pathology was portal hypertension caused by a Chiari-Budd syndrome due to phlebosclerosis of the hepatic and portal veins and their tributaries. Thrombosis was present in these veins and was also found in small veins of the lungs and myocardium. The liver showed changes related to this condition, and was also the seat of an anemic infarct. The spleen exhibited a fibro-adeny.

Case 3. A 50 year old white housewife presented herself in May, 1947, because of nervousness and irritability. She gave a history of having had a cholecystectomy 10 years ago. For the past few months she had been having slightly elevated temperatures (up to 99.4° F.) On examination she had a blood pressure of 210/130 mm. of Hg, a mouth temperature of 100° F. and a pulse of 90. The eyegrounds showed a grade one retinopathy. Fluoroscopy of the chest revealed an enlargement of the outflow tract of the left ventricle and elongation of the aorta. Palpation of the abdomen did not reveal enlargement of the organs or the presence of a mass. There was no tenderness. The urine was negative for sugar and albumin and contained few white and red cells, and no casts. The diagnosis of essential hypertension was made. The patient was seen again in July, 1948, complaining that she was still running a low grade fever and having mild right upper quadrant pain. She was then hospitalized. Her physical status was essentially unchanged. The temperature varied between 99.2° and 100° F. The urinary findings were the same. On culture the urine showed the presence of a nonhemolytic streptococcus, which was sensitive to 0.04 unit of penicillin. An x-ray examination of the stomach, duodenum and colon revealed no pathology. On excretion urography the impression was gained that the left renal pelvis and lower calyces were slightly compressed and displaced to the left. However, this area was partially obscured by bowel contents and was poorly vis-

ualized. No retrograde pyelography was performed. Patient was treated with penicillin and was discharged after 15 days. It was suggested that another intravenous pyelogram be performed in a short time. The patient was not seen again until October, 1950, when she presented herself with weakness and shortness of breath on exertion. Her blood pressure was 210/115 mm. of Hg, the physical findings were unchanged, and again no masses were felt in the abdomen.

In November, 1950, she was again hospitalized because she stated that she had passed three black stools the day before. On admission there was marked pallor of the mucous membranes. A large, hard spleen was felt, the lower pole being about 6 cm. below the costal arch. The blood count revealed the following picture: hemoglobin, 5.4 gm.; red blood cells, 2,230,000; white blood cells, 6,800; reticulocytes, 2.7 per cent; hematocrit, 19 per cent; color index, 0.75; mean corpuscular volume, 85 cubic microns; segmented leukocytes, 77 per cent; nonsegmented, 1 per cent; eosinophils, 1 per cent; basophils, 2 per cent; lymphocytes, 13 per cent; monocytes, 6 per cent. Moderate microcytosis, macrocytosis and poikilocytosis were seen. The platelets were numerous. A bone marrow puncture revealed moderate erythroid hyperplasia. The serum total protein was 7.6 per cent, the albumin, 3.7 per cent and the globulins, 3.9 per cent. The total serum cholesterol was 152 mg. per cent, with 75 per cent esters. The thymol turbidity and flocculation were normal; the cephalin flocculation was 3 plus. The fasting blood sugar was 92 mg. per cent; blood urea nitrogen, 19 mg. per cent. Serum amylase and lipase were normal. The urine contained no sugar or albumin, and the urobilinogen was less than 1:20 positive. An x-ray examination of the gastrointestinal tract was negative, and no esophageal varices were demonstrated. The stools showed a persistently positive guaiac test. The patient's spleen increased in size rapidly on a day-to-day examination, and the diagnosis of a splenic vein thrombosis with bleeding from gastric veins was made. Surgery was recommended. Several blood transfusions were given and on December 12, 1950, the region of the spleen was exposed through a thoraco-abdominal approach. The spleen was found to occupy most of the area opened. It was very firm and paler than normal, and all of its normal ligamentous attachments were occupied by large vascular channels. As division of these was carried out the spleen was observed to enlarge further, making it evident that the splenic vein was obstructed. With this evidence a very rapid splenectomy was performed to prevent complete obliteration of the wound by the growing organ. When the clamps were removed from the specimen, blood escaped under high pressure from the vessels of the pedicle. A search of the splenic pedicle failed to reveal any splenic vein. The artery was doubly ligated and transfixed. A mass was then easily apparent in the region of the tail of the pancreas and of the left adrenal gland. Dissection for the removal of this tumor progressed to the point at which it was found that the mass was intimately attached to the aorta and that the left renal artery and the adrenal gland lay within the mass, but the left kidney was uninvolved. A biopsy was taken in the approximate center of the tumor. The wounds were closed in layers and the patient left the operating room in good condition. The postoperative course was uneventful and she was discharged on the twelfth postoperative day. She was followed as an outside patient. The last check-up was in November, 1952. Her condition has been satisfactory. The hypertension remained unchanged.

The specimen of the spleen weighed 574 gm. The splenic vein was occluded by a thrombus. Histologically, it exhibited a severe chronic passive hyperemia with fibrosis. The biopsy specimen from the mass revealed dense fibrous tissue infiltrated by many lymphocytes and large mononuclear cells. In several areas small lymphoid follicles were seen (figure 5). Small arteries with thick walls were incorporated in the chronic granulation tissue.

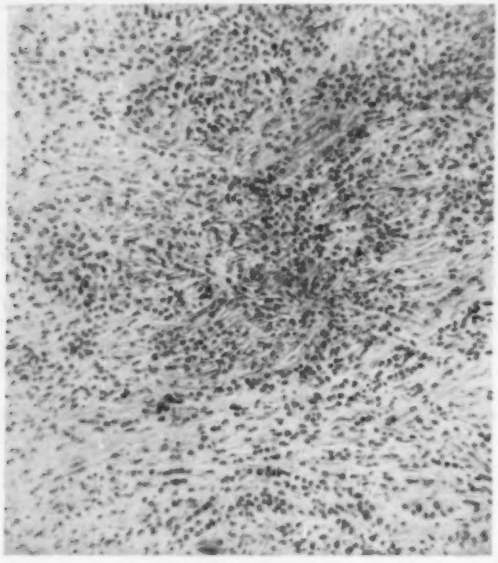


FIG. 5. *Case 3.* Photomicrograph of granulation tissue from retroperitoneal space (× 140). Hematoxylin and eosin stain.

Comment: A chronic inflammatory mass of the left upper retroperitoneal region caused thrombosis of the splenic veins with hypertension in its tributaries which led to bleeding from gastric varices.

DISCUSSION

All three cases described here were primarily referred to one of us (O. C. J.) for surgical relief of the portal hypertension which had been diagnosed before and which seemed to present the main problem in the clinical management. In the first case systemic infestation with *Cryptococcus neoformans* (Torula) was found. The biology of this organism has been reviewed by Conant [19] and Benham,[20] and the morphology and cultural behavior of the material obtained in our case correspond well to observations of other workers. It is known to infest the central nervous system, in particular the meninges and the brain, and numerous such cases have been observed on all continents. Reviews have been written by several workers which adequately characterize this aspect of the infection.[21, 22, 23 and others] Systemic torulosis of any type, but particularly without involvement of the central nervous system, is considerably less frequent and is rarely recognized clinically. Levin,[24] Cox and Tolhurst [22] and Voyles and Beck [25] have listed the following organs as being involved by the fungus: bone, lungs, liver, spleen, pancreas, aorta and lymph nodes. Skin involvement has been studied

by Cawley, Grekin and Curtis.[26] A leukemoid reaction has been observed [27] and occasional association with Hodgkin's disease reported.[28, 29] Adrenal insufficiency with this disease has been noted.[30] Clinically, there is noted a certain similarity to histoplasmosis, which has also an affinity to lymph nodes, occurs in association with leukemias [31] and occasionally invades the adrenals.[30]

Involvement of the intra-abdominal lymph nodes was specifically mentioned by Levin [24] and Voyles and Beck.[25] To our knowledge, in none of these cases was portal lymph node involvement observed. In our case it was apparently present, although it might have played a minor rôle in obstructing the vein in view of the coexistence of hepatic cirrhosis. The latter was quite similar to the type described by Mallory [32] and designated as toxic or postnecrotic cirrhosis. It has been assumed to follow massive hepatic necrosis of various etiologies. In our patient the cause of the cirrhotic process was not established. There was no history suggesting an episode of hepatic necrosis, or any cause thereof. One has to consider the possibility that the overwhelming infection with cryptococcus played a rôle, although no organisms were found in the liver. Its presence in the peritoneal fluid might have been due to breakdown of lymph nodes or to actual subperitoneal involvement. The portal hypertension was verified by the presence of ascites and the congestive splenomegaly, in which a thrombosis of a medium sized vein was found. Esophageal varices were seen at autopsy, and the massive bleeding must have occurred from their rupture. The low platelet count and the hypoprothrombinemia were unquestionably contributory causes of the hemorrhage. The severe anemia was due to hemorrhage, and the presence of spherocytes strongly suggested an additional hemolytic process. Unfortunately, no further studies were made to elucidate its nature. Autopsy of the brain was not permitted. The negative spinal fluid would speak against a central nervous system involvement.

The second case presented in this paper concerned a young female whose portal hypertension was due to phlebosclerosis which led to thrombosis of various branches of the portal tree and also the hepatic veins. Phlebosclerosis of the portal tree as a disease entity has been recognized and its morphology described repeatedly. According to one report [33] it occurred in eight cases out of 61 patients with chronic diseases of the portal and splenic veins. The anatomy of the venous wall in this condition was studied by Li,[35] and its clinical symptomatology, its relationship to "Banti's syndrome" and the pertinent literature were surveyed.[15, 34] Its occurrence in children has been reported by Wilson and Lederer [16] and Freund and Schick.[17] The etiology of this condition seems to be manifold. In older publications syphilis seemed to play a major rôle.[10] Li [35] places great importance upon hypertension in the portal tree leading to thickening of the wall. Some evidence for this assumption was suggested by thickening of the portal vein in cases of liver cirrhosis,[35] and by some experimental work [37] which described phlebosclerosis after reversed Eck's fistula operations in

animals. This sequence is also suggested by the observation of Wilson and Lederer [16] that phlebosclerosis was associated with a congenital narrowing of the portal vein. Inflammatory changes also have been considered by Li. The case presented by us is unusual in many aspects. It is astounding that our patient had no clinical manifestations whatsoever until the first hemorrhage appeared about three weeks before her death. Nevertheless, the involvement was extensive. From the histologic appearance the process must have been quite old, possibly of months' or years' duration. The sclerosis involved also the hepatic veins, producing the Chiari-Budd syndrome, as reviewed by Hirsh and Manchester.[38] The changes in the liver were secondary to the interference with the blood flow through the hepatic veins, and resembled the pathology observed after ligation of the hepatic veins in animals.[39, 40, 41] The changes in the spleen are compatible with those observed in portal hypertension, although such changes may occur without it.[47]

There was no evidence of any inflammatory disease in the abdominal cavity or in the pelvic region to explain the venous changes. Syphilis was not present. There were no signs of polycythemia or an increased platelet count in our patient, and their existence prior to our observation was unlikely. The obstruction of the hepatic veins seemed older than the thrombosis of the portal tree. Nevertheless, we do not believe that the changes observed in the latter were due to hypertension alone because other cases (e.g., in liver cirrhosis) exhibit a much higher portal pressure over a longer period of time without such pronounced thickening of the portal vein wall and/or thrombosis. Moreover, the involvement of veins in other organs would point to the action upon the venous walls of some factor, possibly congenital, the nature of which remains obscure. Our case resembles somewhat the one reported by Reich [43] in a female of the same age.

In the third case presented here the hypertension was confined to the tributaries of the splenic vein, and no evidence was present for an involvement of the main branch of the portal vein. The cause of the splenic obstruction by thrombosis was evidently a retroperitoneal chronic inflammatory mass of undetermined origin. Because of the close topographic proximity of the mass to the tail of the pancreas an old inflammatory process of the latter (possibly dating back to the cholecystectomy) could be related to its formation. Any other origin would be a matter of pure speculation. Chronic pancreatitis had been found to be the cause of portal obstruction,[33] and other inflammatory conditions in the abdomen, unlike those in our patient, have been listed.[13] A phlebitis of the splenic vein resulted from the granulomatous process in its proximity and led to a thrombosis with its sequelae.

Summary

Three cases of portal system hypertension with unusual etiologies are described. The first case was caused by systemic infestation with *Cryptococcus neoformans* (Torula), without demonstrable involvement of the cen-

tral nervous system. The portal hypertension was produced by a coexisting toxic hepatic cirrhosis and also by compression of the portal vein by granulomatous lymph nodes, infested with cryptococcus. The second case concerned a young female with extensive phlebosclerosis of the hepatic and portal veins, leading to thrombosis and the clinical picture of portal hypertension. The third case involved a splenic vein thrombosis caused by a large retroperitoneal chronic inflammatory mass of unknown etiology. All three cases had in common profuse hematemesis, splenomegaly and profound anemia as leading clinical manifestations.

ACKNOWLEDGMENT

Miss Helen MacLean, Chief Bacteriologist, Department of Microbiology, Michael Reese Hospital, performed the studies on the *Cryptococcus neoformans* in case 1.

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TRAUMA IN RELATION TO CORONARY THROMBOSIS: A CLINICAL STUDY OF 42 CASES OF CORONARY THROMBOSIS FOLLOWING TRAUMA OR UNUSUAL EFFORT *

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Considerable interest has been shown recently in the question of causal relation of trauma to coronary thrombosis and myocardial infarction. The answer may be difficult and sometimes impossible, especially in preëxisting coronary artery disease, or in compensation claims, because of the unreliable histories often given by the claimants. Relatively few cases illustrating this relationship have been reported in the literature, and the views expressed by these investigators, based on variable criteria, are often divergent and controversial. It is therefore felt that a review of the pertinent literature and a critical analysis of an additional number of such cases might be of benefit to those interested in this subject. With the foregoing considerations in mind, an attempt will also be made to outline briefly the factors involved in the pathogenesis of coronary thrombosis, to indicate criteria for causal relationship between trauma and coronary thrombosis, and, finally, to discuss the clinical and medicolegal implications of trauma in relation to coronary thrombosis.

Material and Criteria

The clinical material for this study consists of 42 cases of coronary thrombosis and myocardial infarction following trauma seen on the Medical Service (Cardiac Section) of the Bronx Veterans Administration Hospital, and in private consultations for the State Insurance Fund, in New York City. One hundred five cases, with a history of acute "heart attack" following trauma, were examined and the records carefully studied in regard to diagnosis and causal relationship. Among these there were 42 cases of acute coronary thrombosis and myocardial infarction with antecedent trauma or effort of various types—e.g., blow to the chest, gunshot wound within the chest, severe or unusual physical strain or emotional stress, heavy meal, etc. The rest of the cases were due to rheumatic, syphilitic, hypertensive and/or arteriosclerotic heart disease, complicated by acute myocardial insufficiency, pulmonary edema, pulmonary embolism, auricular fibrillation or other arrhythmias, anginal syndrome and coronary insufficiency. The diagnosis was made on the basis of a history of trauma preceding the coronary occlusion, clinical findings and electrocardiographic changes. The selected

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cases presented an opportunity to evaluate the effect of the physical and psychic factors on the development of coronary thrombosis and to investigate their causal relationship.

The following criteria were used in determination of causal relationship between trauma and coronary thrombosis:

1. History of trauma, physical effort or emotional strain, not compatible with usual occupation or habits, preceding acute coronary thrombosis and myocardial infarction.
2. Immediate onset of cardiac symptoms following the alleged injury, or gradual and continuous development of such symptoms or signs during a reasonably short time interval (hours-days).
3. Established clinical diagnosis of acute coronary thrombosis and myocardial infarction corroborated by electrocardiographic evidence.

Review of the Literature

A review of the literature reveals that there are two schools of thought concerning the relationship of trauma to coronary thrombosis. One group of investigators believes that coronary thrombosis almost invariably occurs in the absence of effort, usually at night, and often in the early morning hours, when the blood pressure is low and the coronary blood flow diminished. Some observers maintain that angina pectoris is almost always precipitated by effort or excitement, and that these factors are related to "coronary insufficiency" in about half the cases but are insignificant, rare and coincidental in the production of coronary thrombosis.[1-5]

A second group of observers holds a different point of view. Oppenheimer [6] states that he frequently sees cases in which sudden, exceptionally heavy physical exertion is followed by good evidence of coronary occlusion, and he is therefore compelled to accept causal relationship between an accident and coronary thrombosis. He also believes that trauma to the chest, with or without contusion to the chest wall, can undoubtedly precipitate coronary occlusion, and that there are instances in which it is difficult to deny relationship between severe psychic trauma and coronary thrombosis. Fitzhugh and Hamilton [7] studied 100 cases of fatal angina and coronary occlusion directly following unusual, violent or prolonged physical exertion or strain, and reported two examples of causal relationship in their cases: "An elderly woman, who had angina on exertion for two years, stayed well within her effort limits for many months, but was drawn to her garden the first warm day of spring. She worked hard and steadily all morning and afternoon with shovel, rake, and trowel. Soon after dinner she had a coronary occlusion." The second case is that of "a man, age 50, who traveled 150 miles to watch boat races. He drank much alcohol, and fell in the water from which he was helped out. He then ran for his train and caught it, but immediately had a coronary occlusion from which he did not recover." A

similar, very convincing case was cited by Boas: "A hotel manager, age 45, fell while playing ball. A few minutes later he began to experience precordial oppression and difficulty in breathing, and soon broke out in a cold sweat. The pain persisted for several hours until he received an injection of morphine, but the oppression lasted the whole night. The heart sounds were faint, the rate rapid. The blood pressure was 84 systolic. Two days later the heart appeared enlarged and a precordial friction rub was heard. The electrocardiogram revealed a classical picture of infarction of the left ventricle. Two weeks later a right hemiplegia and aphasia occurred suddenly." Boas [8, 9] is of the opinion that trauma and bodily effort may directly induce closure of a coronary artery with cardiac infarction, or initiate the syndrome of angina pectoris. Kissane,[10] reviewing the effects of nonpenetrating chest injuries in traumatic heart disease, states that while there is always a possibility of coincidental occurrence of coronary artery occlusion, too many cases of chest injury have been followed by this condition to call them coincidental.

In discussing the psychosomatic aspects of coronary artery disease, Arlow [11] outlined the implication of an acute emotional trauma, and illustrated the relationship to coronary occlusion by the following unusual example: "A subway motorman, with an excellent service record, inadvertently drove a train past a switch during the height of the rush hour, failing to notice the proper signal. He succeeded nevertheless in stopping the train and telephoning the control station in time to avoid a serious accident. After the danger was over he developed pain in the chest with breathlessness, and died three days later." Weiss [12] emphasized the importance of emotional factors in the etiology and aggravation of coronary heart disease, and related the following case: "A 40 year old, nervous, white male who had considerable difficulty with his employer, decided to get even with him and, while riding in a bus to his place of employment, he suddenly experienced chest pain. He was then taken to a hospital where a diagnosis of posterior wall myocardial infarction was made." Here, Weiss believes, "the constant nervous tension and resentment culminated in an acute emotional state which apparently was the factor responsible for the coronary occlusion." Katz [13] likewise regards an emotional episode as a possible trigger mechanism in patients with coronary sclerosis: atheromatous material may be released during such an episode and form a clot within an artery, or a resulting severe or prolonged coronary insufficiency may lead to ischemia and infarction of the myocardium.

Pathogenesis of Coronary Thrombosis

The view expressed by some observers, that physical effort or stress may frequently be related to "coronary insufficiency" and only rarely to coronary thrombosis, is not substantiated by clinical studies correlated with pathologic findings. It is well known that prolonged coronary insufficiency may lead

to anemic necrosis and infarction of the myocardium, the outcome depending upon the degree and duration of the myocardial ischemia as well as on the efficiency and the reserve of the collateral circulation of the coronary arteries. Too many factors are involved in the mechanism and pathogenesis of coronary thrombosis to permit a sharp clinical distinction between coronary insufficiency and coronary thrombosis. Some of these factors will now be briefly reviewed.

Paterson [14] and Winternitz [15] demonstrated the presence of vascularization of the intima in atheromatous arteries, and stressed the importance of intimal and intramural hemorrhage in the development of atherosclerosis and its complications. Wartman [16] pointed out that a large intramural hematoma may block the lumen of an artery, either by its size or by rupture through the intima leading to thrombosis of the vessel. Rupture of atheroma within the coronary arteries was also observed by Leary.[17] Similar findings were reported by Horn and Finkelstein [18] as a result of their

TABLE I

Anatomic and Hemodynamic Factors in Coronary Thrombosis

A. Coronary Atherosclerosis

Fibrotic thickening and vascularization of intima
Intimal hemorrhage—atheroma—thrombosis

B. Blood Pressure Variations and Biophysical Changes

1. Rise in blood pressure (acute emotional stress)
Intimal hemorrhage / Tear in atherom. wall } Intravascular hemorrhage or release of atherom. material } Vascular occlusion

Increase in hematocrit and blood viscosity / Decrease in sed. rate, coagul. and prothrombin times } Thrombosis

2. Fall in blood pressure (mental depression, shock):
Diminished blood flow—stasis—thrombosis

studies of the mechanism of coronary occlusion in arteriosclerotic arteries; they stated that an intramural hemorrhage in a sclerotic artery may cause massive intimal hemorrhage and act as a precipitating agent in the formation of a thrombus. Clark, Graef and Chasis [19] examined sections of thrombotic coronary arteries and observed fresh breaks in the fibrous lining of the plaques, with blood extravasation into the atheroma. Cooksey [20] believes that extreme rise in blood pressure during sudden severe physical exertion may cause a subintimal hemorrhage or tear in the wall of the hardened vessel, while a fall in blood pressure may produce stasis and disturbance in the coronary circulation precipitating thrombosis. Selye and Fortier,[21] discussing the response of the body to stress situations, described increased capillary permeability and hemorrhage, hemoconcentration, hypertension or hypotension (depending upon the intensity of the stress) during the A.R. (alarm reaction) of the G.A.S. (general adaptation syndrome). Schneider [22] studied the effects of exercise and emotional stress on the biophysical properties of the blood, and demonstrated that these factors produced a rise in

blood pressure with an increase in blood viscosity and hematocrit, a decrease in sedimentation rate and coagulation and prothrombin times. These observations, summarized in table 1, clearly show the influence of physical and emotional factors on the vascular tone and the clotting mechanism of the blood.

Analysis of Cases and Results

Forty-two cases were studied. The ages of the subjects varied from 33 to 67 years; the majority were between 50 and 60 years, indicating that trauma in middle aged or elderly individuals is most likely to precipitate coronary thrombosis or aggravate a preëxisting coronary heart disease. There were remarkably few cases of malingering. All patients had been seen previously by physicians, either privately or in hospitals; the diagnosis was made clinically and corroborated in each case electrocardiographically; the posterior or posterolateral type of infarction predominated in the findings.

Table II

Causal Relationship in 42 Cases of Coronary Thrombosis Following Trauma or Unusual Effort

Causal Relationship	No. of Cases	Per Cent	Criteria
1. Definite (+)	13	30.9	a. History of trauma or unusual strain preceding coronary thrombosis
2. Possible (+?)	6	14.3	
3. Doubtful (?)	5	12.5	
4. Nonexistent (0)	18	42.3	b. Onset of symptoms immediately or shortly following injury.
			c. Clinical and electrocardiographic diagnosis of coronary thrombosis and myocardial infarction.

The causal relationship in the selected 42 cases of post-traumatic coronary thrombosis was evaluated on the basis of the previously outlined criteria, and, according to results, was determined as (1) definite (+); (2) possible (+?); (3) doubtful (?); (4) nonexistent (0). In the appraisal and classification of the cases, special consideration was given to the time interval between trauma and onset of symptoms, the nature and severity of the alleged trauma, the degree of the physical or emotional strain involved, and its relation to the usual occupation, work or habits of the subject. The results and criteria used are reported in table 2, and several illustrative cases are presented.

For comparison, the experiences of other investigators in this problem were reviewed from the literature and their results tabulated in chronologic order (table 3). The variability of the data is apparently due to the different criteria used by these authors and the clinical material they studied. The evidence of causal relationship between trauma and coronary thrombosis will of course be higher in a selected group of post-traumatic cases than in a general series of cases of coronary thrombosis.

CASE REPORTS

Case 1. A 51 year old saleslady was struck in the chest by a carton weighing about 75 pounds which fell from an upper shelf while she was trying to reach it. She was able to push it off her chest, but soon felt a sharp pain in the precordial region. Although the pain persisted, she continued working for two days. On the third day, however, the pain in the chest became severe and a physician was called who administered a hypodermic and advised hospitalization.

When seen by me two weeks later at a local hospital in New York City, the patient appeared pale and acutely ill, and complained of chest pain and weakness. The first apex sound was muffled; no friction rub or gallop rhythm was heard. The lungs were clear. The hospital records revealed a skin discoloration on the upper left chest. The blood pressure was 100/60 mm. of Hg. The temperature was 99.8° to 101.0° F. The sedimentation rate (Westergren) was 96–104. Two electrocardiograms were taken and the findings were as follows:

1. (Taken three days after the accident) Small R wave in V_2, QS in V_6, inverted T waves in Leads I, V_{5-6}, low T in aVL.
2. (Taken six days later) QS also in V_2, with elevated S-T segment (3 mm.), inverted T wave in aVL and V_{5-6}, iso-electric T in Lead I.

Comment: The history and findings justify the diagnosis of an acute coronary thrombosis with anterior wall myocardial infarction. The sudden onset of the symptoms, the continuous chest pain and the course of the disease following the injury indicate causal relationship between the trauma and the acute coronary thrombosis. The effect of the chest blow, and possibly of the emotional upset, cannot be denied. The occlusion apparently developed slowly, becoming complete on the third day following the injury.

Case 2. A 53 year old laborer, with no previous symptoms of heart disease, stated that on August 16, 1951, while shoveling dirt off a road with a heavy, deep shovel and throwing it into a truck, he was suddenly seized with a burning sensation in the chest accompanied by a feeling of choking, and broke out in a cold sweat. He was unable to continue his work and was taken home, where he received emergency treatment by his physician. An electrocardiogram taken the next day showed a "heart attack," and he was admitted to a hospital in Mt. Kisco, in Westchester County, where he was treated for several weeks. A consultant confirmed the diagnosis of acute coronary thrombosis with posterior wall myocardial infarction.

The serial electrocardiograms showed successive changes as follows: *August 17:* Prominent Q waves and upright T waves in Leads II and III. *August 20:* Deeply inverted, cove-plane type T waves in Lead III; prominent, tall T wave in V_2, and inverted T waves in V_{5-6}; Q_2 and Q_3 persisted. *October 25:* An electrocardiogram taken by me revealed deep Q waves in Leads II and III, diphasic T wave in Lead II, and inverted T wave in Lead III. The QRS-interval measured 0.11 second, the intrinsicoid deflection was widened in V_2, and there was an R-R′ present in the same chest lead.

Comment: These findings are consistent with a recent posterolateral wall myocardial infarction with incomplete right bundle branch block due to acute coronary thrombosis. Causal relationship may be recognized if the history is confirmed by investigation. The onset of the symptoms and the course of the disease are possibly related to an unusual and severe physical exertion in a previously healthy individual.

Case 3. A 54 year old shipping clerk with a history of a previous heart attack while lifting and wrapping heavy parcels suddenly felt a severe pain in the epigastric region and in both arms, associated with difficulty in breathing and cold perspiration. He was unable to continue his work and was admitted to the Bronx Hospital, where he was treated with oxygen.

Examination at the hospital showed the heart sounds muffled. The blood pressure was 118/64 mm. of Hg. Sedimentation rate was 28–68 mm. per hour. White blood count was 11,900. The electrocardiograms showed the following findings:

1. (Three days after the accident) Prominent Q_2 and Q_3; T_2 slightly inverted; T_3 moderately inverted.
2. (Ten days after the accident) T_3 moderately inverted; T_2 deeply inverted, and T_1 tall, prominent; Q waves in Leads II and III.
3. (Eighteen days after the accident) T_2 and T_3 less inverted; T_1 less prominent.

Comment: The history and findings are consistent with an acute coronary occlusion and posterior wall myocardial infarction. However, the onset of the attack during usual work and the history of a previous heart attack indicate the possibility of spontaneous occurrence of coronary thrombosis in this case; unless the investigation will show that the effort was unusual at the time of the attack, causal relationship is doubtful, depending on further evidence.

Case 4. A 36 year old white male with a history of previous myocardial infarction two years prior to this accident ate a heavy lunch and then was painting the walls of an apartment when he developed crushing substernal pain associated with retching and vomiting, and was admitted to the Veterans Administration Hospital in the Bronx. The heart sounds were muffled. Blood pressure was 114/80 mm. of Hg; white blood count, 20,000; sedimentation rate, 19 mm. per hour. Several electrocardiograms were taken which showed the following findings:

1. Prominent Q_3, depressed S-$T_{1 \text{ and } 2}$, elevated S-T_3; absent R in V_1 and V_2; small Q in V_2; depressed S-T in V_{4-6}; occasional premature ventricular contractions.
2. Marked serial changes in S-T segments and in Lead III; an intraventricular conduction defect (widening of QRS) appeared with serial changes in aVF and Leads II and III.

Comment: The diagnosis of acute coronary thrombosis with posterior wall myocardial infarction is well established. The painting of the walls following a heavy meal in a patient with coronary heart disease may be considered an unusual, severe effort which precipitated the attack of coronary thrombosis.

Case 5. A young white male was wounded in action in Belgium in September, 1944, and sustained multiple wounds due to foreign bodies in the left chest, shoulder, left arm and hand. Physical examination revealed scars in the anterior chest and left shoulder. Electrocardiogram showed QS in V_2 and V_3 and deep Q wave in V_4 and V_5, with inverted T waves in V_4. Fluoroscopy showed a metallic body pulsating within the heart in the septal region. Diagnosis: Findings are consistent with posterior and anterior wall myocardial infarction.

Comment: This obviously is a case of direct cardiac injury due to gunshot wound, which resulted in coronary thrombosis and myocardial infarc-

tion of the anterior and posterior wall with septal involvement. (Case was published in this Journal.[21])

Discussion

The results of this study and the data reported by other observers (table 3) show that the occurrence of coronary thrombosis following trauma is not rare or coincidental, as some investigators would have us believe. The incidence of coronary thrombosis related to trauma in this series (Group 1) is 30.9 per cent. To be sure, the number of cases of coronary thrombosis preceded by trauma is relatively small as compared with the general high incidence of coronary occlusion; nevertheless, even if numerically low, it is a definite and important clinical and medicolegal problem in certain instances, and should not be disregarded because of statistical data. It is rather re-

Table III

Trauma in Relation to Coronary Thrombosis

Name of Authors—References	All Cases Studied	No. of Causal Relationship Cases	Per Cent of Causal Relationship Cases	Remarks
1. Fitzhugh and Hamilton[7]	100	57	57%	In all cases unusual effort preceded coronary thrombosis; in some cases effort was violent.
2. Boas[3, 26]	25	13	52%	Personal observation.
3. Cooksey[30]	100	17	17%	Personal observation.
4. Smith et al., Ann Int. Med. **17**:681, 1942	100	32	32%	Physical exertion, severe emotional upset.
5. French and Dock, J.A.M.A. **124**:1233, 1944	80	26	35%	Coronary thrombosis occurred after vigorous exertion.
6. Phipps, C., J.A.M.A. **106**:761 (Mar. 7) 1936	437	175	40%	Coronary thrombosis occurred after physical stress

grettable that the rôle of trauma as a precipitating or aggravating factor in heart disease is so often underestimated or overlooked and the cardiac damage resulting from it unrecognized. This attitude on the part of some physicians is difficult to comprehend in view of the injurious effects on the cardiovascular system caused by the industrial hazards, frequent accidents and constant strain of modern living. Several reasons might perhaps account for it: (1) the complex nature of the relation between trauma and heart disease and the special problems involved in the individual cases; (2) the lack of generally accepted criteria for causal relation between injury and heart disease; (3) the difference of opinion among physicians in this field.

Cardiac injuries may be of several types: (a) direct or penetrating injury, e.g., stab or gunshot wound, fractured rib, chest surgery; (b) indirect or nonpenetrating chest injury, e.g., boxing, fall, blow, compression or steering-wheel injury, airplane crash, explosion; (c) severe, unusual physical exertion or emotional stress (psychic trauma). The damage to the heart may consist of structural lesions, functional disturbances, or both.

It is generally conceded that a penetrating or nonpenetrating chest injury may cause serious damage to a coronary artery and precipitate coronary thrombosis, with or without myocardial infarction. Much controversy, however, exists among investigators regarding the causal relation of an antecedent physical effort or unusual emotional stress to coronary occlusion. Some of the opponents of such relationship [5] recently pointed out that coronary occlusion, in the overwhelming majority of cases, occurs when the subjects are at rest or during the night; that it is a spontaneous event, and that therefore activity plays an insignificant part in the causation of the disease. Furthermore, they maintain that coronary insufficiency and coronary thrombosis can be differentiated clinically and electrocardiographically, and that the former is frequently related to trauma, but the latter only rarely and coincidentally. In support of their view these authors refer to reported findings of subintimal hemorrhages in patients who died of causes other than coronary thrombosis, thus denying the view predominant among investigators, that hemodynamic factors play an important rôle in the mechanism of coronary thrombosis and myocardial infarction following trauma.

The validity of their arguments, however, is questionable for the following reasons. The belief, based on statistical data, that the relation of trauma to coronary occlusion is purely fortuitous has been disproved by the observations of Blumgart,[23] Sprague,[24] Boas [25] and others, and by the results of observations reported in this study. Moreover, the contention that coronary insufficiency can be distinguished from coronary thrombosis by clinical and electrocardiographic findings is similarly debatable. Clinically, it is often impossible to state when prolonged coronary insufficiency ends and when myocardial damage, necrosis or infarction begins. Transitions from functional disturbances to organic cardiovascular lesions are not uncommon; in fact, the development of a myocardial infarction is usually associated with the preliminary stages or zones of ischemia and injury which, if the collateral circulation is efficient, are reversible, but otherwise may lead to the formation of necrosis and infarction. Electrocardiographically, it is well known that a negative record does not exclude myocardial damage. Furthermore, RS-T segment elevation and Q waves may be absent in lateral wall or intramural myocardial infarction.[26, 27] The electrocardiogram, in midlateral infarction, may show RS-T depression and T inversion in Leads I, II and V_4, and in an intramural infarction, a loss of R/S progression (drop in R voltage between two chest leads of higher voltage) and/or T wave changes may be the only diagnostic abnormality. A similar view is expressed by Barker,[28] who believes that "it is impossible, mainly from electrocardiographic standpoint, to differentiate an occlusion of a coronary artery as against non-occlusive and transitory insufficiency," and that in a number of cases myocardial infarction may occur with T wave changes only. Friedberg [29] likewise recommends caution in the clinical diagnosis of "coronary failure" (coronary insufficiency), "for attacks of this type are often premonitory of

myocardial infarction, or represent cases of coronary occlusion with localized infarction which do not produce striking changes in a routine electrocardiogram." Blumgart [23] also challenges the thesis that effort, physical or emotional, does not play a precipitating rôle in certain cases of coronary occlusion. He feels that in a small but definite number of cases these factors may place an additional strain on the coronary circulation, and produce subintimal hemorrhage or rupture of an atheromatous abscess resulting in a myocardial infarction. Yater [30] reported the findings in various "heart attacks" due to coronary heart disease in young individuals, and concluded that "rest is more favorable for the formation of thrombi than activity but it cannot be denied that activity may play a part in the production of thrombi." No one questions the fact that most cases of coronary thrombosis are spontaneous in origin, but this does not mean that trauma is to be considered as of little importance as a causative factor in coronary occlusion.

It is apparent from these considerations and the analysis of the cases presented that the appraisal of causal relationship of trauma (especially of physical or emotional strain) to coronary thrombosis may be a difficult problem in certain instances. Each case must be evaluated individually and all the facts and findings carefully considered. Much help may be obtained from a thorough history and complete physical examination, including serial electrocardiograms. The history should contain detailed information regarding the nature and severity of the injury, type and amount of work performed during or immediately preceding the attack of coronary thrombosis, and degree of physical or emotional strain involved (as compared with usual effort). Furthermore, environmental conditions, personality pattern of patient, previous injuries or illnesses, and other relevant data should be recorded. The time of the onset of the symptoms, in relation to the alleged injury, is essential and should be noted, although a brief interval (hours-days) may elapse in some cases between the accident and onset of the disease, due to slow development of occlusion, which may initially be partial and gradually become complete. A preëxisting coronary artery disease or a history of previous myocardial infarction does not rule out causal relationship to trauma if there is sufficient evidence of a recent attack of coronary occlusion; on the contrary, the more diseased the heart is, the more easily and more severely it may be damaged by trauma or effort. In fact, it is doubtful whether effort alone ever produces coronary thrombosis in a normal artery.

From a clinical standpoint, the importance of proper diagnosis and recognition of causal relationship between coronary thrombosis and trauma cannot be too strongly emphasized. Adequate treatment may be lifesaving and timely advice helpful in the prevention of future attacks in certain cases, while an error can be disastrous to the patient and cause embarrassment to the physician. When the diagnosis is uncertain as between coronary insufficiency and thrombosis, it is obviously safer to diagnose and treat the case as coronary thrombosis.

Special care is necessary in the examination of cases for causal relationship in disability or compensation claims, in view of the inaccurate or exaggerated statements made by some claimants, and the financial implications. The history may have to be checked by investigation of the record, and the diagnosis based mainly on objective findings and laboratory data. The opinion should, however, be fair but impartial to both the claimant and the insurance carrier. A too liberal or "sympathetic" attitude in such claims, not warranted by the facts and findings, might prolong the disability, prejudice employers against employment of cardiacs in industry, and result in a disservice to the community.

In this brief presentation I have attempted to outline the basic principles involved in the relationship of trauma to coronary thrombosis. The experiences of others and my own in this field have been discussed.

Summary and Conclusions

1. The purpose of this study is to appraise the clinical and medicolegal importance of trauma as a precipitating or aggravating factor in the causation of coronary thrombosis and myocardial infarction.

2. The literature on this subject has been reviewed and the mechanism of trauma in the pathogenesis of coronary thrombosis briefly discussed.

3. Several criteria for determination of causal relationship were suggested: (a) history of trauma or unusual strain (physical effort or emotional stress) preceding the attack of coronary thrombosis; (b) onset of cardiac symptoms immediately or shortly after the injury or effort; (c) clinical and electrocardiographic diagnosis of coronary thrombosis and myocardial infarction.

4. Forty-two cases of coronary thrombosis were selected for this study from 105 cases of acute "heart attacks" stated in the histories; the rest were due to functional disturbances in various types of heart disease, e.g., acute myocardial insufficiency, pulmonary edema, pulmonary embolism, auricular fibrillation and other arrhythmias, anginal syndrome and coronary insufficiency.

5. Causal relationship in the studied cases was determined on the basis of the outlined criteria as definite (+), possible (+?), doubtful (?), and nonexistent (0); the results were presented in table 2.

6. The difficulty in differentiating between coronary insufficiency and coronary thrombosis from a clinical and electrocardiographic standpoint was discussed, and the inapplicability of this principle in determination of causal relation to trauma was pointed out.

7. The frequency of causally related cases of coronary thrombosis in post-traumatic "heart attacks" as it appears from this study is believed to be sufficiently high to warrant consideration of trauma as an important factor in the causation of coronary thrombosis and myocardial infarction in appropriate cases.

8. The clinical significance of the recognition of causal relation of trauma to coronary thrombosis, especially with regard to adequate treatment and possible prevention of the disease, was stressed; and a medicolegal approach to this problem, based on a thorough history, objective findings and impartial attitude, was indicated.

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CASE REPORTS

ENDOBRONCHIAL GEOTRICHOSIS *

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Introduction

The fungus Geotrichum, like Monilia, has been reported to cause a wide variety of pathologic conditions as well as to be a nonpathogen. Tonsillitis,[1] conjunctivitis, bronchitis,[2] cutaneous lesions,[3] ulcerative rectal lesions,[4] pulmonary diseases [5] and septicemia [6, 7] have been attributed to the organism. Two cases of Geotrichum septicemia are reported in an infant and in a debilitated aged individual.[6-7] With these exceptions the English literature has been concerned mainly with bronchopulmonary geotrichosis. In 1934 Smith [8] reported five cases, two pulmonary and three bronchial. In 1946 Kunstadter, Pendergrass, and Schubert [9] reported one case of pulmonary and two of bronchial geotrichosis. Reeves,[10] in discussing the roentgen findings of bronchomycosis in 79 patients, mentioned that two of the group were caused by Geotrichum but gave no details. Thus it is seen that the reported cases are extremely infrequent and that the type of disease caused by the organism is not well defined. It is entirely conceivable that the fungus may be a contaminant only and not by itself a cause of pathologic changes, as certain authors feel is the case with *Candida albicans*. For this reason we feel that all cases in which there is a high index of suspicion of Geotrichum pathology should be reported so that, as the evidence accumulates, a more definite opinion can be formed as to the pathogenicity of the organism and the types of disease which it causes. During the past year we have observed two cases of bronchitis with irrefutable evidence that the etiologic agent was the fungus Geotrichum.

Case Reports

Case 1. This 53 year old Ecuadorean male has been under medical observation at Gorgas Hospital, Ancon, Canal Zone, from 1946 to 1953. He has been a painter with the Panama Canal Company for 33 years.

His first hospital admission was June 28, 1946, because of hemoptysis which had occurred four days before. The hemoptysis consisted of several successive episodes of cough with production of bright red sputum. This had not recurred prior to admission. There had been a similar instance six months previously which was studied elsewhere with no positive findings. Physical examination revealed hypertension only. Complete blood count, urinalysis, sedimentation rate and serology were normal. Chest x-rays were essentially negative. Ear, nose and throat examinations revealed no bleeding point in the nose, pharynx or larynx. Four sputa and one gastric washing were negative for acid-fast bacilli on smear and culture. The patient was discharged 15 days later without a definite diagnosis.

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From the Medical Service, Gorgas Hospital, Ancon, Canal Zone.

His next admission was February 9, 1950, for the same complaints. On January 23 he had noted a tight feeling in his chest with a productive cough. That night he was awakened with cough and expectorated two teaspoonfuls of bright red blood. While in the hospital the cough and bleeding persisted intermittently for a few days and subsided spontaneously. The patient was afebrile and had no systemic symptoms. Physical examination was negative again. Six sputa and three gastric washings were negative on smear and culture for tubercle bacilli. Routine laboratory studies were normal. Chest x-ray was negative. The patient was discharged on February 14, again without a definite diagnosis.

He was re-admitted on February 20 because the cough and hemoptysis recurred and persisted. Every day he produced from 2 to 4 ounces of bloody sputum ranging from dark to bright red. This was associated with apprehension and weakness. His temperature ranged daily between 98° F. and 100° F. Bronchoscopy was done on March 2 (Dr. R. Rea), and the report was as follows: "Trachea appeared normal. The carina appeared broadened and gave the impression of some resistance. The right main stem bronchus was normal in caliber, the mucosa was pale, slightly edematous and contained white exudative patches which bled easily. The orifice of the upper lobe was visualized and was normal; the orifices of the right lower lobe and middle lobes were hyperemic and contained small amounts of the purulent secretion. The orifice of the left main stem bronchus was normal in size and there were similar exudative patches present." Specimens were taken from each bronchus and scrapings from the exudative patches. The impression was a low grade exudative bronchitis. The histologic sections of the above specimens revealed fungi which morphologically resembled Geotrichum; the pathologist's impression was bronchitis due to fungus, type unspecified. Cultures done were positive for the genus Geotrichum. On March 18 the patient was started on intravenous sodium iodide (35 gm. total) and on oral saturated solution of potassium iodide, 20 drops three times a day. On March 22 it was stated in the chart that there was less coughing and less blood streaking. On April 1 there was no more hemoptysis and very little coughing. Repeat bronchoscopy on March 30 showed only hyperemia of the bronchial mucosa. The patient was afebrile from April 1 through the remainder of hospitalization. Hematologic studies and chest x-rays were repeatedly normal. Bronchoscopy was done again on April 3 and the report was as follows: "The right main stem bronchial mucosa appeared somewhat more hyperemic than normal but decidedly improved over previous examinations. There was a minimal amount of thick material in the bronchial lumen. The upper lobe orifice was normal, the middle and lower lobe orifices appeared normal. The mucosa of the left main stem bronchus appeared similar to the right but there was less secretion." The impression was healing bronchitis much improved over previous examinations. Cultures from secretions and scrapings were negative for acid-fast bacilli and fungi. The patient was discharged from the hospital on May 10, 1950, and followed with periodic visits to the Chest Clinic. He had no complaints of cough or expectoration until December 20, 1952, when he again had a sudden episode of coughing up about a cupful of bright red blood and was re-admitted to the hospital. Physical examination revealed temperature, pulse and respiration to be normal. Blood pressure was again noted to be elevated. Chest x-ray was negative. Routine blood studies were within normal limits. Six sputum and five gastric washes were negative for acid-fast bacilli, and fungi. A bronchogram was done and revealed normal filling bilaterally. Bronchoscopy on January 14, 1953 revealed both main bronchi and secondaries to be normal in appearance with the exception of the right lower lobe bronchus which appeared somewhat roughened on the posterior wall. Its color was normal throughout and there was no secretion or evidence of bleeding in the bronchial tree. The patient was discharged after this to be followed in the Chest Clinic.

Case 2. This 54 year old white male had had numerous previous admissions to Gorgas Hospital for hypertensive and arteriosclerotic heart disease with episodes of cardiac insufficiency. His last admission was in December, 1952 with acute pulmonary edema. The unusual features of this admission were a red atrophic tongue and a distressing cough which was productive of a very peculiar looking sputum. Each coughing spell produced a teaspoonful of brownish red sputum which was extremely tenacious, mucoid and odorless. The mucoid appearance was remarkable, and in general the sputum resembled that of a Friedländer's infection. Studies of the sputum revealed only pneumococci until a direct smear with potassium hydroxide was done on January 14, 1953, when innumerable spores of Geotrichum were found. Culture of this sputum gave luxuriant growths of Geotrichum. Frequent chest x-rays at this time revealed no evidence of parenchymal disease. Bronchoscopy was contemplated but was deferred on the basis of the patient's poor general condition. On January 15 saturated solution of potassium iodide was begun, 5 drops three times a day, with a gradual daily increase until 40 drops three times a day were given. Within a few days the sputum lost its rusty color, became more abundant and was less mucoid. Within three weeks the cough subsided, and attempts to obtain Geotrichum on smear and culture were unsuccessful. During the second week in February there was a recurrence of paroxysmal attacks of left ventricular heart failure; coma and death followed on February 10.

The body had been embalmed prior to autopsy. Grossly and microscopically the lungs and bronchi appeared normal. There was remarkable coronary arteriosclerosis, with multiple and recent myocardial infarctions and evidence of cardiac insufficiency.

Comment

The first case illustrates the importance of bronchoscopy in arriving at a diagnosis in so-called "chronic bronchitis" or "hemoptysis of unknown etiology." To our knowledge this is the first description of the bronchoscopic picture of endobronchial lesions due to Geotrichum.

The finding of the organism in sections of the scrapings of the bronchial mucosa during bronchoscopy is a most unusual feature in this case and leaves no doubt of the etiology of the observed lesions. Since there was no evidence of pulmonary parenchymal involvement, bronchoscopic follow-up was an excellent means of observing regression of the disease under therapy.

The second case is one of a severe heart disease with a complicating acute bronchitis. The sputum in this case had an unusual appearance, remarkably like that described by Smith [2] in bronchial geotrichosis. Geotrichum spores were easily identified on direct examinations and grew abundantly on culture. These facts, plus the response to potassium iodide, substantiate the diagnosis of bronchial geotrichosis. Unfortunately, the condition of the patient was such that a bronchoscopy was contraindicated. Necropsy failed to reveal any endobronchial or pulmonary disease, and we may attribute this to iodide therapy, although evaluation at autopsy was extremely difficult due to previous embalming.

Summary

1. The literature on Geotrichum infections is briefly reviewed.

2. Two additional cases of endobronchial geotrichosis are presented. Iodide therapy appeared to be beneficial in both cases.

3. The endobronchial lesions as seen by bronchoscopy are described. An unusual feature was the finding of the organism in the bronchial scrapings.

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LÖFFLER'S SYNDROME FOLLOWING USE OF A VAGINAL CREAM *

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EVIDENCE indicating that Löffler's syndrome is a manifestation of an allergic reaction in the lung tissue is steadily accumulating. From the time of its original description by Löffler [1] in 1932, this syndrome of transitory pulmonary infiltrations associated with blood eosinophilia received much attention in European countries; it has been only in the past five years that American medical literature has reflected an equal degree of interest.

Löffler and his co-workers [2] reproduced the syndrome in the guinea pig by the administration of ascaris eggs, and early reports stressed the relationship of this syndrome to parasitic infestation,[3, 4, 5, 6, 7] especially ascariasis, amebiasis, trichinosis, filariasis and hookworm infestation. Emphasis shifted away from the parasitic etiology when Herbut and Kinsey [8] in 1946 produced the syndrome in rabbits sensitized to horse serum by instilling horse serum intratracheally. Jahiel and Jahiel [9] in 1950 likewise succeeded in producing the syndrome in rabbits by intrapulmonary sensitizing doses of autogenous antigen followed by intravenous shocking doses.

The specific allergen responsible in individual clinical cases is not often identified. Engel [10] in 1935 identified the privet plant pollen as the responsible allergen in a group of cases in China. Ragweed pollenosis has been indicted,[11, 12] as have Prontosil,[13] sulfadiazine,[14] para-aminosalicylic acid [15] and penicillin.[16, 17]

The following case report is considered of special interest in that a clinical

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picture compatible with Löffler's syndrome followed upon the vaginal instillation of a sulfonamide cream and recurred after each of three subsequent applications of the drug.

Case Report

The patient, a 48 year old white unmarried woman, was first seen at the Sidney Hillman Medical Center in August, 1951, for a routine medical examination. There

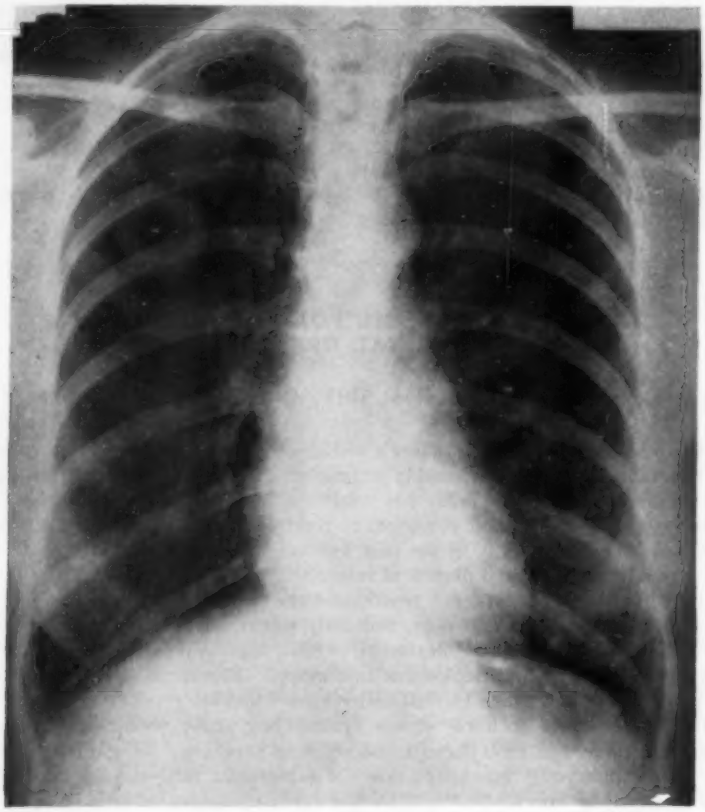


Fig. 1. Chest roentgenogram of August 7, 1951 (two months prior to onset of illness). No significant abnormality other than linear fibrosis at right apex.

were no complaints other than a moderate leukorrhea, which had been present for an indeterminate period of time. Systemic and past history was negative. No evidence of allergy was elicited. The only point of interest in the family history was that the patient's mother had died of pulmonary tuberculosis in January, 1950; the patient had been in close contact with her. Physical examination was negative. Laboratory work, which consisted of a chest x-ray (figure 1), complete blood count,

urinalysis and serology, revealed no significant abnormality. The gynecologist to whom the patient was then referred found a hymenal ring ulcer and prescribed daily vaginal instillations of AVC Improved,* a preparation containing 9-aminoacridine, sulfanilamide and allantoin with lactose in a water-miscible base.

The patient was next seen at her home on October 6, 1951. She had been taken ill on the previous day with chills, fever of 100° to 103° F., slight cough, generalized

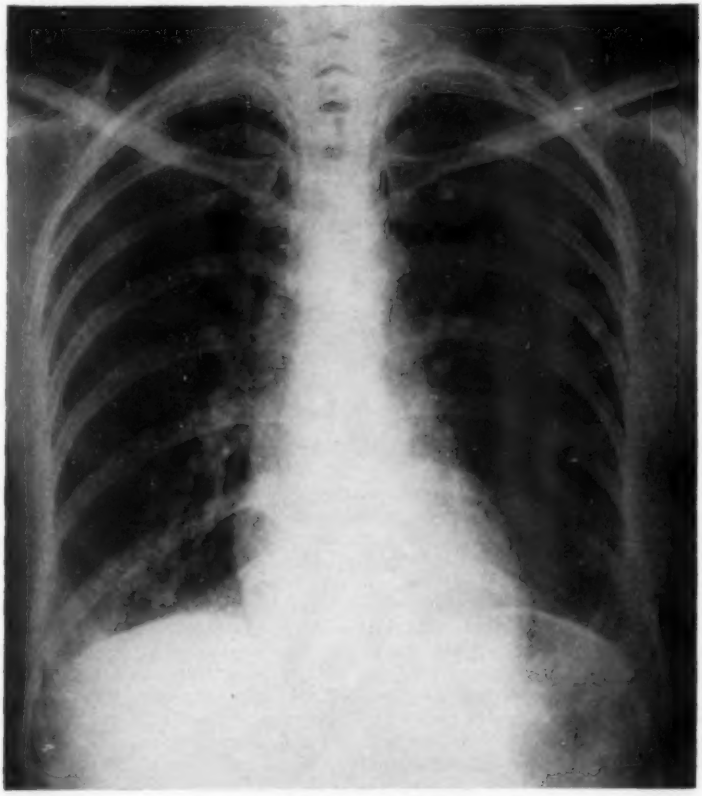


FIG. 2. Chest roentgenogram of October 30, 1951. Pulmonary infiltrations most clearly seen at right second anterior interspace and right base. No change in right apical fibrosis.

abdominal and muscular pains, especially across the costal margins bilaterally, and nausea and anorexia. Examination was negative except for the fever, generalized abdominal tenderness and several small bilateral axillary nodes. The lungs were clear. Three hundred thousand units of procaine penicillin were given intramuscularly, as well as Terramycin (500 mg. every six hours the first day, followed by 250 mg. every six hours for the next two days), and supportive therapy. All symptoms disappeared in four days.

* The National Drug Company, Philadelphia.

The patient was again seen at her home on October 18 because of the recurrence of symptoms that morning. The clinical picture appeared identical. The temperature was 103° F. There was a marked amount of muscular, costal and abdominal pain. A more troublesome dry cough was present, and the patient complained of a feeling of pressure and heaviness over the chest. Again the lungs were clear and the rest of the examination was negative. Another injection of procaine penicillin was

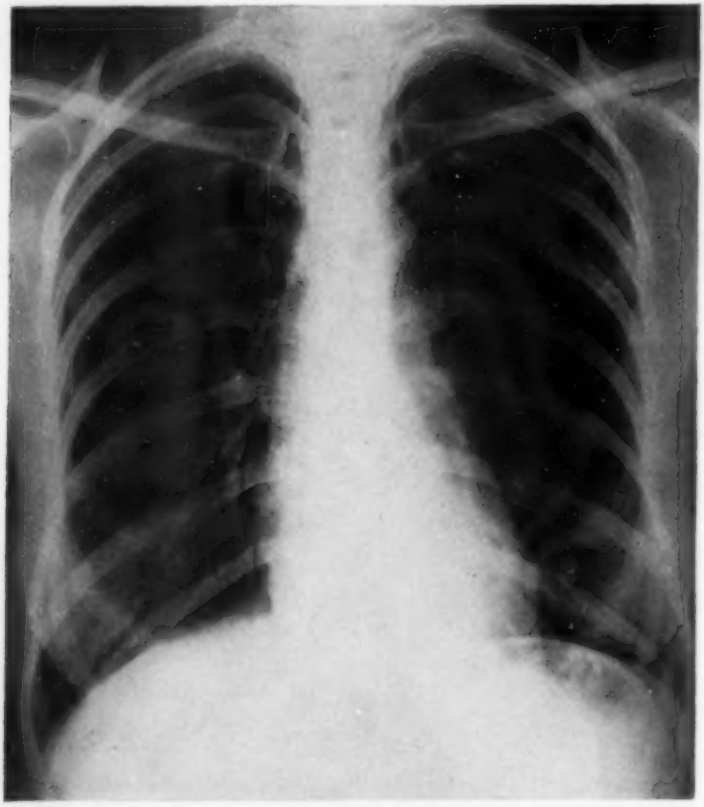


FIG. 3. Chest roentgenogram of November 10, 1951. Previous infiltrations have completely disappeared.

given and supportive measures were prescribed, and again recovery was uneventful over the next four days.

One week later the patient reported back to the Clinic. She had no complaints and revealed no abnormal findings; chest x-ray and blood count were normal. Three days later (October 29), there was a sudden onset of chills, fever, cough and muscular pains, and she was immediately hospitalized for study. Admission examination revealed transient râles at the right base posteriorly, and fever of 102° F. The white blood count was 27,050, with 75 per cent polymorphonuclear leukocytes and 18 per

TABLE I

Peripheral Blood Studies

Date	Total WBC per cu. mm.	Eosinophils %	Total Eosinophils per cu. mm.
Aug. 7	5,800	2	116
Oct. 28	6,500	3	195
Oct. 30	27,050	18	4,869
Nov. 1	11,900	46	5,474
Nov. 3	8,600	58	4,988
Nov. 5	7,200	32	2,304
Nov. 9	4,350	7	304
* Nov. 14	14,750	11	1,622
Nov. 15	9,600	26	2,496
Nov. 17	8,100	46	3,726
Nov. 20	5,750	20	1,150
Nov. 30	7,600	3	228

* Blood specimen drawn the morning following the provocative test dose of vaginal cream.

cent eosinophils. Sedimentation rate was 41 mm. per hour. Chest x-ray the following morning revealed soft infiltrations sparsely scattered throughout both lungs, more prominent at the right second anterior interspace and base (figure 2); the roentgen picture was considered compatible with either an atypical pneumonia or an allergic reaction. The possibility of tuberculosis could not be ruled out.

Migratory râles were audible for only the first two days, and cough and other symptoms gradually subsided by the fourth day. Chest x-ray was repeated in five days and showed almost complete resolution of the pneumonitic process. One week later complete resolution was reported (figure 3). In the meantime, blood studies revealed progressively more marked eosinophilia, reaching a peak of 58 per cent (table 1). Blood culture, febrile agglutinations, cold agglutinins, and heterophil antibody and cephalin cholesterol flocculation studies were all negative. Sputum smear and culture were negative for tubercle bacilli. Mantoux test was negative to first strength PPD and 2 plus to second strength. Skin test with trichinella antigen was negative, as was stool examination for ova and parasites.

The eosinophilia naturally directed attention to a possible allergic situation. The past history was completely negative from this standpoint. On careful review of the activities and exposures of the patient preceding each of these episodes, one factor was found common to each: the use of the vaginal cream prescribed in September. The patient had first used the cream on September 26 and 27, and then stopped it because of a trip out of town. Its use was resumed on October 3 and 4; then, due to the onset of illness on October 5, it was again discontinued. Use of the cream was started again on October 17, and discontinued when she became ill on the following day. The cream was used for the fourth time on the morning of October 29; she became ill that evening (table 2).

TABLE II

Relationship between Onset of Symptoms and Time of Drug Instillation

Time of Drug Instillation	Onset of Symptoms
Sept. 26 and 27	—
Oct. 3 and 4	Oct. 5
Oct. 17 (a.m.)	Oct. 18 (a.m.)
Oct. 29 (a.m.)	Oct. 29 (p.m.)
* Nov. 13 (2 p.m.)	Nov. 13 (8 p.m.)

* Provocative test dose during case study.

The very suggestive relationship between the use of the vaginal cream and the onset of symptoms was then tested more critically by having the patient instill another dose of the cream intravaginally. This was done on November 13 at 2 p.m. Approximately six hours later the patient complained of a heavy, tight feeling in the chest, chills, cough and muscular pain. Her temperature rose rapidly to 102° F., and transient wheezes were heard over the chest. By the following morning her white count had risen to 14,750, with 11 per cent eosinophils, and a sputum specimen obtained that day revealed 40 to 50 per cent of the cells present to be eosinophils. Because of the extreme discomfort of the patient, any remaining cream was removed by vaginal douching the morning after this last instillation. Migratory râles were heard for approximately two days; all symptoms abated and she became afebrile within four days. Aspirin, codeine and Pyribenzamine were the only drugs used during this last episode. Chest x-ray was disappointing in that no actual infiltrations were seen except for the fibrosis at the right apex seen in all her films and which, in view of the negative first strength tuberculin test and lack of change, was not considered of clinical import. This may possibly have been related to the abbreviated period of exposure to the cream due to the vaginal douching.

Because of the correlation between instillation of the vaginal cream and the episodes described above, an effort was made to test for the specific constituent of the cream responsible for the patient's reaction. Scratch and patch tests were performed with each of the nine components * of the preparation by Dr. Phillip Gottlieb, allergist at the Sidney Hillman Medical Center. The only one that yielded a positive skin reaction was lactic acid. No reaction was elicited with either the allantoin or sulfanilamide.

Discussion

The association between the vaginal instillations of AVC Improved and the acute episodes described above seems too definite to be ascribed to chance alone. It is interesting to note that no clinical manifestations followed the first use of the drug, but that with each subsequent application there was a progressive shortening of the time interval between use of drug and appearance of symptoms (table 2).

Results of the skin tests were disappointing. However, skin testing of drugs is notoriously inadequate and inaccurate. Sufficient controls should be run to know the significance of the positive reaction to the lactic acid. Despite the negative reaction, we do not feel that the possibility of a sensitivity to sulfanilamide can be ruled out. The patient does not recall ever having been given a sulfonamide medication previously. Intravaginal testing rather than skin testing would have been most interesting but was not feasible.

Although the pulmonary infiltrations as seen on x-ray were not migratory in nature, this case was most likely an example of Löffler's syndrome, the antigen having been one of the constituents of AVC Improved (possibly sulfanilamide). The route of sensitization was the vaginal mucosa. The generalized muscular pains plus the nausea and vomiting indicate that the lungs were not the sole site of the hypersensitization reaction. This is in accord with the belief of certain investigators like Harkavy [18, 19] and Ehrlich and Romanoff [20] that, although attention has been focused primarily on the pulmonary findings in so-called Löffler's syndrome, the concept of this syndrome should in fact be broadened.

* Samples for tests were kindly supplied by The National Drug Company, Philadelphia: triethanolamine, lactic acid (50 per cent), diglycol stearate, propylene glycol, allantoin, sulfanilamide, 9-aminoacridene hydrochloride, stearic acid (lumps), lactose.

It should rather be recognized as a comparatively mild type of systemic allergic disease in which the lungs happen to be the site of most prominent reaction.

Summary

A case of Löffler's syndrome which developed following the use of a sulfonamide-containing vaginal cream is described. The allergic nature of Löffler's pulmonary infiltration and eosinophilia is now recognized, and cases where the specific allergen is suspected are slowly accumulating. We believe this is the first case to be reported where the vaginal mucosa was the route of sensitization.

Acknowledgment

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BENIGN HYPERGLOBULINEMIC PURPURA: CASE REPORT*

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THE term hyperglobulinemic purpura was introduced by Waldenström [1] in 1943 to describe three patients with an unexplained increase in serum globulin, high sedimentation rate, and purpura of many years' duration. He recognized the benign nature of the condition and excluded the diagnosis of multiple myeloma, which shows several similar features. Since this initial observation, additional cases have been reported in the European literature (table 1). There have been no reports in American journals of similar cases. In this article we present a case report of a patient with hyperglobulinemic purpura who has been observed for 10 years; we also briefly summarize the literature.

CASE REPORT

A 49 year old housewife whose chief complaint was "bleeding" of 10 months' duration was first seen in March, 1944. In February, 1942, she had been hospitalized elsewhere with type 4 lobar pneumonia, acute cholecystitis and acute pancreatitis. She had responded to treatment with specific pneumococcus serum, and cholecystostomy had been performed. The hospital records indicated that at that time there had been no significant anemia, albuminuria or pyuria. Plasma proteins had not been measured.

In the summer of 1943 the patient first experienced recurring episodes of slight swelling of the ankles, small "red spots" of the lower extremities, and periodic gingival bleeding. The development of purpuric spots seemed to be precipitated by prolonged standing or by the wearing of tight undergarments. Hematologic studies in August, 1943, were reported to have shown a mild anemia, normal platelet count and normal coagulation studies.

Physical examination on admission in March, 1944, disclosed a well nourished woman who was not acutely ill. The temperature and pulse rate were normal, and the blood pressure was 130/86 mm. of Hg. There was slight pallor of the skin and mucous membranes. Scattered petechiae and purpuric lesions were present over the lower extremities and appeared similar to the lesions of Schamberg's syndrome (figure 1). The purpura was most evident around the calves and ankles. No pretibial edema was present. The retinal vessels revealed no significant change. The tourniquet test (Rumpel-Leede) was negative. The liver and spleen were not

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From the Department of Medicine, Cleveland Clinic, and The Frank E. Bunts Educational Institute, Cleveland, Ohio.

TABLE I

Author	Case	Age	Sex	Duration of Purpura in Years	Total Serum Protein	Albumin	Globulin	Fibrinogen	Electrophoretic Analysis Relative % Gamma Globulin	Cryoglobulin	Sedimentation Rate	Anemia	Hemorrhagic Studies	Additional Findings
Waldenström[1,8,9]	1	60	F	19	8.7	3.4	4.7	0.6		0	↑	+	N	Sternal marrow does not resemble myeloma.
	2	62	F	14	9.5	4.2	5.3		48	0	↑	+		
	3	36	F	10	9.8	4.1	5.7		43	0	↑	+		
Waldenström[8,9]	4	27	F	4	9.7	4.8	4.9		41	0	↑			
Waldenström[9]	5	23	F	14	9.8	3.4	6.4			0	↑	+	N	
	6	33	F	12			↑			0	↑	+	N	
	7	66	M	10	7.9		↑			0	↑	+	N	No x-ray evidence of myeloma.
Curtz[2]	8	63	F	3	8.35	4.14	4.21				↑	+	N	Marrow exam. shows sl. shift leukocytes to left and without significant pathologic changes.
Humerfelt[3]	9	58	F	8	8.35	3.14	5.21				↑	+	N	Normal marrow. Bence Jones negative.
Lindeboom[4]	10	76	M	5	9.5	3.9	4.9	0.7			↑	+	N	—
Oberste-Lehn[5]	11	31	F	8	11.0	3.1	7.9		61	0	↑	+	N	Light colored inclusion bodies in mature and immature plasma cells. Not diagnostic multiple myeloma.
Horster[6]					12.1	3.9	8.2		75					
Linke[7]	12	48	M	4	7.5	3.4	4.1		33	0	N	0	N	Bence Jones negative.
Case presented	13	59	F	10	9.6	3.13	5.64	0.8	43	0	↑	+	N	No increase plasma cells. X-rays skeletal system normal. Bence Jones negative.

palpable. The remainder of the physical examination was normal. Roentgen examination of the chest and skull gave normal findings.

The laboratory studies revealed the urinalysis to be normal. The hemoglobin concentration was 9.3 gm. per 100 c.c. (Haden-Hauser), the erythrocyte count was 3,650,000 per cubic millimeter, and the hematocrit reading 30 c.c. per 100 c.c. of blood. Wright-stained films presented a conspicuous basophilic background, with moderate anisocytosis and rouleau formation of the erythrocytes. The leukocyte count was 3,950 per cubic millimeter, with 62 per cent neutrophils, 31 per cent lymphocytes,



FIG. 1. Purpuric lesions of the lower extremities.

1 per cent eosinophils, 5 per cent monocytes and 1 per cent basophils. The icterus index was 3. The platelet count was 340,000 per cubic millimeter (Rees-Ecker method). The bleeding time was 2 minutes (Ivy method) and the coagulation time 13 minutes (Lee-White method). The prothrombin time was normal. The sedimentation rate was 1.8 mm. per minute by the Rourke-Ernstene method (normal values below 0.5 mm. per minute). The blood urea, urea clearance, blood sugar, serum calcium and serum phosphorus were normal. The blood Wassermann and Kahn reactions were negative. Bence Jones proteinuria was absent.

The total plasma proteins were 9.6 gm. per 100 c.c. The electrophoretic (Tiselius) protein analysis revealed albumin, 3.13 gm.; alpha globulin, 0.58 gm.;

beta globulin, 0.97 gm.; gamma globulin, 4.09 gm.; and fibrinogen, 0.83 gm. (figure 2). The gamma globulin comprised 42.7 per cent of the total proteins, compared with the normal range of 9 to 14 per cent.

The Wright-stained films of the marrow obtained by sternal aspiration were hypocellular. The myeloid-erythroid ratio was 3 : 1. Megakaryocytes were scant but showed no significant cytologic change. The granulocytes revealed a slight shift to the left. The plasma cells were mature and averaged 3 to 5 per cent. The reticuloendothelial cells, histiocytes and macrophages were slightly increased in number. Atypical mononuclear cells with lightly stained chromatin nucleus and pale cytoplasm were conspicuous. They showed basophilia of the periphery of the cytoplasm and could not be classified. The marrow was not characteristic of multiple myeloma.

The diagnosis remained obscure but an atypical manifestation of multiple myeloma was suspected. Progress observation two years later, in June, 1946, re-

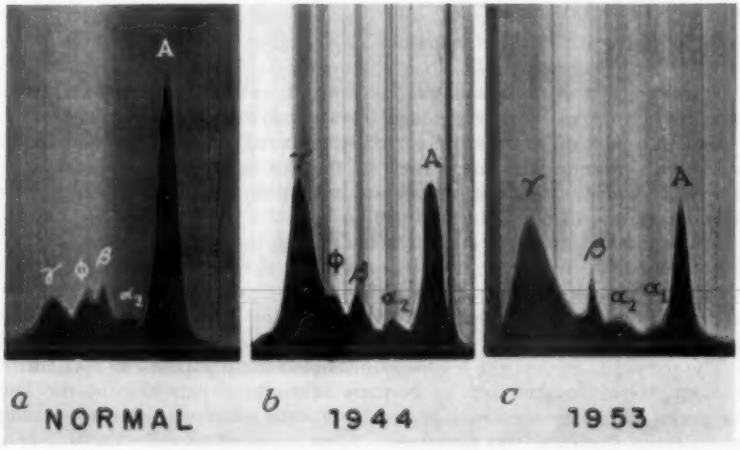


FIG. 2. (a) Normal plasma—PO_4 buffer pH 7.8. (b) Patient's plasma 1944—PO_4 buffer pH 7.8. (c) Patient's serum 1953—Veronal buffer pH 8.6.

vealed no significant subjective or objective changes in the patient's condition. The findings of urinalysis, hematologic studies, electrophoretic plasma protein examination and roentgen examination were similar to those in 1944. The blood urea was 36 mg. per 100 c.c., and the urea clearance was 40 per cent in the first hour and 47 per cent in the second hour. The marrow aspirate appeared the same.

The patient was recalled for follow-up study in October, 1952, at which time there was no apparent change in the subjective symptoms of occasional gingival bleeding and purpura of the lower extremities. The patient believed the purpura was aggravated by cold weather as well as by prolonged standing. Complete physical examination disclosed no significant change except increase of pallor and slight elevation of the blood pressure (to 148/90 mm. of Hg). Roentgen examination of the chest and skull remained normal.

The urinalysis was normal except for the presence of a trace of albumin. Bence Jones proteinuria was absent. The sedimentation rate was 0.75 mm. per minute. The urea clearance was 56 per cent in the first hour and 50 per cent in the second hour, with a blood urea of 33 mg. The bromsulfalein retention was 2 per cent in

45 minutes. The cephalin-cholesterol flocculation was 2 plus in 48 hours. The thymol turbidity was 10 units. Cold agglutinins were absent. The hemoglobin concentration was 8.0 gm. per 100 c.c.; the erythrocyte count, 2,960,000 per cubic millimeter, and the hematocrit, 26 c.c. per 100 c.c. The leukocyte count was 6,100 per cubic millimeter, with a normal differential. The Wright-stained blood films appeared similar to previous studies. The platelets were estimated to be normal. The icterus index was 4. The bleeding time was 3.5 minutes and the coagulation time was 9 minutes. The prothrombin time was normal. The plasma lupus erythematosus test (Haserick) was negative.

The total serum proteins were 12.6 gm. per 100 c.c. Electrophoretic protein analysis revealed albumin, 3.56 gm.; alpha-1 globulin, 0.49 gm.; alpha-2 globulin, 0.86 gm.; beta globulin, 1.16 gm.; gamma globulin, 6.53 gm. The gamma globulin formed 51.8 per cent of the total serum protein. Special studies failed to reveal the presence of cryoglobulin. Study of the sternal marrow aspirate revealed no significant change since 1944.

Discussion

The absence of an acceptable diagnosis in this case is obvious. The patient is now 59 years of age, and for the last 10 years the recurring episodes of purpura of the lower extremities have not seriously impaired her health or physical activity. The prominent abnormalities in the laboratory data include an extremely high gamma globulin, rapid sedimentation rate, mild chronic anemia and moderate impairment of renal function.

A summary of the most important findings in the cases reported to date is presented in table 1. There are 10 women and three men, with ages ranging from 23 to 76, with an average age of 49 years. One of the patients (case 11) was reported dead at the end of five years' observation from exhaustive bronchitis and diarrhea.

The purpuric lesions which usually prompted these patients to seek medical treatment were characterized by periodic showers of petechiae in the lower extremities, and were often precipitated by unusual exertion, prolonged standing and excessive pressure from garments. After repeated episodes the skin of the legs revealed a residual mottled brown pigmentation which was probably hemosiderin. The reported patients had purpura from two to 19 years, with an average of 9.3 years. Similar types of purpura are rarely observed in patients with multiple myeloma.

In all of the reported patients with hyperglobulinemic purpura in whom electrophoretic studies were performed the elevated serum globulin was the result of a marked rise in the gamma globulin. In one of the patients (case 10) the gamma globulin comprised 75 per cent of the total serum protein, about seven times the normal expected value. Waldenström [9] was impressed by the observation that the gamma globulin seemed to remain elevated for a period of years. There is little quantitative alteration in the other serum proteins. In the present case report the gamma globulin was extremely high upon initial study and showed a slight rise during the nine years of observation. The serum albumin was slightly below normal values and the fibrinogen was slightly elevated. The rapid sedimentation rate might be the result of either the increased globulin or fibrinogen.[10] Waldenström [1] reported that one of his patients (case 2) had a rapid sedimentation rate for 20 years.

Patients with cryoglobulins may manifest purpuric lesions on exposure to cold as a result of increased viscosity and precipitation of the cold globulins in the small surface blood vessels. Cryoglobulins have not been detected in the reported cases of hyperglobulinemic purpura.

The presence of a mild to moderate anemia has been reported in all cases except one. The anemia was normocytic and normochromic in type and refractory to the usual forms of treatment. The leukocyte counts showed no significant deviation from normal. None of the reported cases revealed specific coagulation defects or thrombopenia. Liver function studies of our patient and several reported cases were within the range of normal. Slight changes in some of the flocculation tests were considered to result from the altered protein patterns.

Repeated sternal marrow aspirations in our case were hypocellular, and the minor cytologic changes observed may have been due to the elevation of the serum globulin. Horster [6] described light-colored inclusion bodies in mature and immature plasma cells, and suggested that they represented a pre-crystalline form of the gamma globulin. In spite of the small number of patients reported, the evidence indicates that the marrow examinations exclude the diagnosis of diffuse myeloma but fail to clarify the etiology of the condition.

No specific cause has been found for the marked increase of gamma globulin in our patient or in the reported cases. Waldenström [9] suggests the possibility of a chronic virus infection stimulating antibodies and increasing the gamma globulin. He also discusses the hypothesis that the derangement in globulin metabolism causes a deficiency of some globulin fraction necessary for normal capillary resistance. Lindeboom [4] speculates that allergy may cause the increased gamma globulin and the purpura. Schmengler and Esser [11] favor the theory that an allergen causes the alteration of gamma globulin which, in turn, adversely affects the capillary endothelium.

None of the proposed concepts of the etiology and mechanism of this disorder has been proved. Repeated observations of our patient over a 10 year period fail to offer any significant clues to the basic cause of the condition. Necropsy studies have not been reported due to the infrequency and benignity of the disorder.

Summary

1. Periodic observations for 10 years of a patient with hyperglobulinemic purpura are presented and the literature is briefly summarized.

2. This disorder is characterized by a long benign course with relapsing purpura, marked increase in the gamma globulin, rapid sedimentation rate, mild anemia and absence of a defect in blood coagulation.

3. No evidence of multiple myeloma has been found for long periods of observation.

4. The cause of the condition is unknown, so the descriptive term of "benign hyperglobulinemic purpura" was introduced by Waldenström.

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CORTISONE TREATMENT OF OCULAR PALSY IN SARCOIDOSIS *

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The occurrence of cerebral nerve palsies in patients suffering from sarcoidosis has recently been emphasized by Longcope and Freeman.[1] Facial paralysis, diplopia, strabismus, partial ptosis of the eyelids, either unilateral or bilateral, pupillary changes, involvement of the sensory portion of the trigeminal nerve, central deafness, dysarthria, paralysis of the vocal cords and of the soft palate, loss of taste, hypesthesia of one side of the tongue and dysphagia have all been encountered.

Colover [2] recently reported three cases of sarcoidosis in which various cranial nerves were involved. In one there was bilateral facial palsy with ageusia. In another there were disturbed taste sensation, bilateral facial paralysis, dysphagia, weakness of the palate, paralysis of the right vocal cord, wasting of the right trapezius muscle and right ophthalmoplegia. In the third case unexplained fever, amenorrhea and somnolence existed for two years before a positional nystagmus developed. Ventriculography revealed dilatation of the entire ventricular system. Exploration revealed an adhesive arachnoiditis which, when biopsied, yielded sarcoid tissue. Of the 118 cases of sarcoidosis with central nervous system involvement that Colover reviewed, 58 had peripheral facial palsies; 31 had optic neuritis; 29, dysphagia; nine, vocal cord paralysis; eight, nerve deafness; four, vestibular nerve disturbances; six, ptosis; three, third nerve palsies; two, sixth nerve paralysis; one, fourth nerve palsy; five, sensory

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loss or impairment in the trigeminal area of the face; three, lost corneal reflexes; seven, weakness of the tongue, and two, anosmia.

Although there are numerous instances of spontaneous remissions of sarcoid lesions none has been so dramatic as those following the administration of cortisone. Sones et al.[3] and Goldston et al.[4] in 1951 and Siltzbach in 1952 [5] reported numerous cases in which prompt resolution of sarcoid lesions was noted following institution of cortisone or ACTH therapy. No effects of cortisone upon sarcoid ocular palsies were noted. The following case is therefore reported.

Case Report

A 26 year old colored male accountant was first seen in an Army hospital in 1946 because of symptoms of peptic ulcer. Physical examination at that time revealed

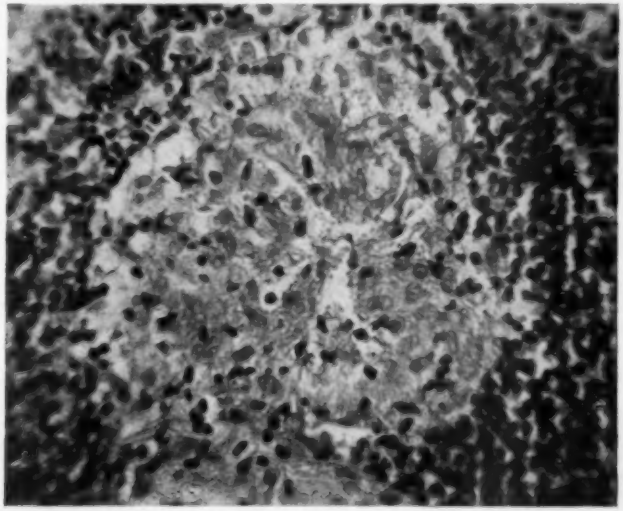


Fig. 1. Biopsy specimen from posterior cervical lymph node. × 305.

enlarged postcervical lymph nodes, one of which when removed for biopsy revealed sarcoid tissue (figure 1). A gastrointestinal series demonstrated the presence of a duodenal ulcer. On a rigid ulcer régime the patient's symptoms subsided.

In December, 1949, he was admitted to the VA Hospital, Fort Howard, Maryland, because of bleeding hemorrhoids. For two months prior to this he had been aware of an aching sensation about and behind the left eye. Following the administration of spinal anesthesia for hemorrhoidectomy he developed persistent headache involving chiefly the left side of the face, and diminished sensation in the left half of his upper lip. This persisted until the time of his second admission, on October 15, 1952. X-ray of the lungs on December 20, 1949, demonstrated increased perivascular markings throughout both lung fields, and prominence of both hilar shadows (figure 2). X-ray of the left great toe revealed punched-out areas of decreased density, measuring approximately 0.5 cm. in diameter, in the proximal phalanx (figure 3).

The patient was re-admitted on October 15, 1952, because of persistent headaches. Although the pain was usually confined to the left side of the face, it occasionally radiated to the suboccipital region and down the back of the neck into both shoulders. It was sharp, throbbing and deep, frequently preventing sleep. Approximately two months prior to this admission he first noticed double vision on looking to the left; this lasted for several hours and disappeared spontaneously. During the following six weeks he had two similar episodes. Five days prior to admission the diplopia reappeared and persisted.

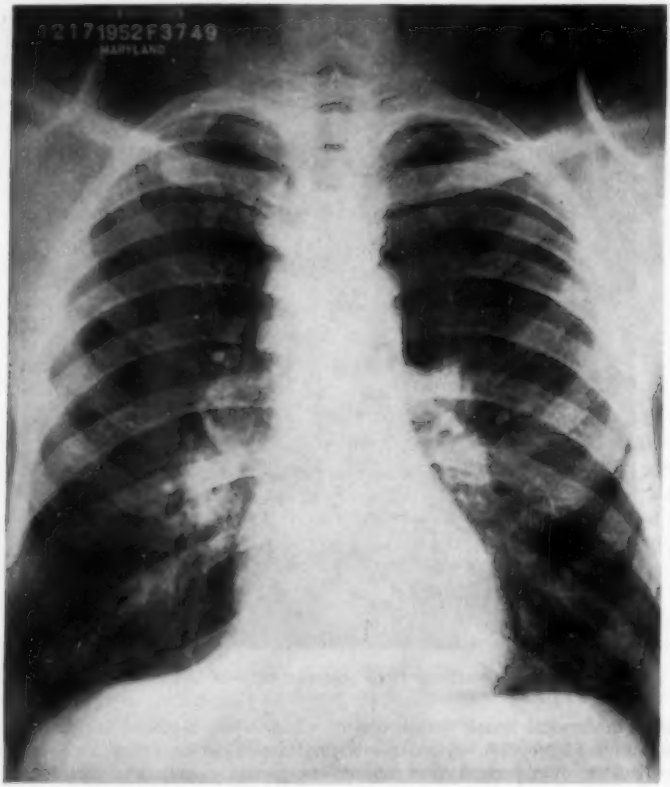


FIG. 2. X-ray of lungs revealing enlarged hilar and superior mediastinal lymph nodes.

Physical examination on admission revealed a well developed and well nourished colored male in no acute distress. A striking degree of left lateral rectus palsy was apparent (figure 4). Hypalgesia was evident in the area of the left trigeminal nerve distribution. Except for scars at the sites of the previous lymph node excisions, the head and neck were normal. The heart and lungs revealed no abnormalities. The blood pressure was 110/56 mm. of Hg. No abdominal viscera or masses were palpated. No lymphadenopathy was apparent. The extremities, genitalia and rectal examination were normal.



FIG. 3. Punched-out areas of decreased bone density in left great toe.

The red blood count was 4,790,000 per cubic millimeter; the hemoglobin, 11.2 gm.; the white blood count, 3,500 per cubic millimeter, with 65 per cent neutrophils and 35 per cent lymphocytes. No sickling of the red blood cells could be demonstrated. The fasting blood sugar was 93 mg. per cent and the urea nitrogen, 10.7 mg. per cent. The serum calcium was 10.2 mg. per cent, and inorganic phosphorus, 5.3 mg. per cent. The serum albumin was 4.3 gm. per 100 c.c., and the globulin, 3.1



FIG. 4. Palsy of left lateral rectus muscle demonstrated on left lateral gaze (November 10, 1952).

gm. per 100 c.c. Urinalysis revealed only a rare white blood cell. The specific gravity was 1.015, and neither albumin nor sugar was present. The Eagle flocculation test was negative. The spinal fluid was clear, and contained 3 lymphocytes per cubic millimeter, 66 mg. per cent of sugar and 29 mg. per cent of total protein. The Wassermann test and gold curve were negative. A Fishberg concentration test revealed a maximal specific gravity of 1.027.

X-ray of the lungs revealed both hilar and superior mediastinal lymph node enlargement, with minimal perivascular infiltration in the midportion of the inner zones of both lung fields. X-ray of the sinuses revealed no abnormalities. On November 12, 1952, approximately one month after the onset of the persistent left lateral rectus palsy, a course of cortisone therapy was instituted. On November 15, after 600 mg. had been administered, a marked diminution in the degree of left lateral rectus palsy was noticed. On November 28, after 1.9 gm. of the drug had been administered, the palsy was no longer apparent (figure 5). The headache, which had been persistent for approximately three years, had completely subsided and only minimal numbness of the left upper lip remained. Cortisone therapy was discon-



FIG. 5. Recovery from palsy after cortisone therapy (November 28, 1952).

tinued on December 8. From then until the time of this report (June 1, 1953), the patient has experienced only minimal numbness of the left upper lip. There has been no suggestion of diplopia, and both eyes move freely in all directions in unison.

DISCUSSION

While it is well known that lateral rectus palsies from any cause frequently remit spontaneously, the prompt and what appears to be permanent remission noted in the foregoing case while under treatment with cortisone makes the course of events seem unlikely to be merely coincidental. It may be readily surmised that this patient with sarcoidosis of at least six years' duration developed granulomatous lesions about the base of the brain and cranial nerves accounting first for the aching sensation behind the left eye, then for the persistent postspinal headache. The diminished sensation experienced in the left half of the upper lip could very well have resulted from involvement of the maxillary division of the left trigeminal nerve. The transient and then persistent paralysis of the left lateral rectus muscle may be interpreted as involvement of the left abducens

nerve. Finally, the recovery from the lateral rectus palsy and headache, with the persistence of minimal numbness of the left upper lip, may be best explained on the basis of resolution of granulomatous tissue about the left sixth nerve and base of the brain with fibrosis involving the maxillary division of the left fifth nerve. In the latter instance, one must assume that irreversible damage must have occurred.

Conclusions

1. A case is presented of persistent left lateral rectus palsy in an individual with generalized sarcoidosis.
2. Cortisone apparently caused a remission of the palsy and the associated protracted headache.
3. An associated numbness of the left upper lip, although reduced in intensity, has remained to date.
4. Cortisone deserves further trials in sarcoidosis associated with central nervous system and/or cranial nerve lesions.

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ACUTE MASSIVE VENOUS OCCLUSION: REPORT OF A CASE SUCCESSFULLY TREATED WITH EXERCISE*

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Prompt treatment of the usual case of thrombophlebitis is always necessary, but with the exception of pulmonary embolization there is usually little threat to life or to the affected extremity.

There is, however, one form of thrombophlebitis which is being recognized with increasing frequency. It presents a more dramatic picture and often threatens life or loss of the involved part. Proper emergency treatment is required to avoid serious complications. Such treatment differs to a great extent from that for simple thrombophlebitis.

This more serious form of venous occlusion has been termed "blue thrombophlebitis" (phlegmasia cerulea dolens),[1] thrombophlebitis with gangrene,[2] or

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gangrene of venous origin.[3] More recently, the term "acute massive venous occlusion" [4] has been applied to the syndrome. This term is preferred, since it more accurately expresses the pathologic changes that exist in this condition: there are actually an acute blockage of all major venous channels and an inhibition of all outflow of blood from the extremity.[3, 4]

Approximately 81 cases of the syndrome have been reported in the literature to date. At least one-half of these patients developed gangrene of the involved extremity and required major or minor amputations. The mortality has been approximately 25 per cent. Since there has been no real agreement upon the basic pathophysiology until recent years, numerous therapies have been suggested. These included vein ligations,[5, 6] thrombectomies,[2] sympathectomies, lumbar paravertebral blocks, or spinal anesthesia.[7, 8, 9] In many instances the correct diagnosis was not made until after the development of gangrene or until an exploratory operation had been performed.[10] This entity has most often been confused with acute arterial occlusion. An excellent review of the subject has recently been published by Haimovici.[3]

In 1951 Veal and his associates [4] described a method of therapy which employs exercise in the treatment of acute massive venous occlusion. This method is practical and logical, and the results appear to be better than those noted after other forms of management.

We have recently observed a case of acute massive venous occlusion of the left lower extremity which presented some interesting diagnostic features and which was treated by exercise, with excellent results.

Case Report

A 61 year old white man was admitted to Walter Reed Army Hospital because of pain in the left calf of five days' duration. The pain had gradually increased in severity and had localized in the left popliteal area.

Physical examination revealed calf tenderness and a positive Homans' sign on the left side. Slight pitting edema without varicosities was present. Pulsations in the femoral, popliteal and posterior tibial arteries were normal. Dorsalis pedis pulsations were absent. Tender cordlike areas could be palpated in the left popliteal area. The remainder of the physical examination was noncontributory. A diagnosis of superficial popliteal vein thrombophlebitis was made, etiology undetermined. The patient was placed on bed-rest and was started on anticoagulant therapy with both heparin and Dicumarol. Oral dibenzyline, 10 mg. four times daily, was given in an attempt to reduce any reflex vasoconstriction that might be present. Reflex heat was applied to the abdomen. Pain and tenderness gradually subsided and, following ambulation, the patient was discharged on the seventeenth day of hospitalization. Elastic support without anticoagulant therapy was advised.

Seven days later, pain in the medial aspect of the left thigh occurred and the patient was re-admitted.

Pitting edema of the left lower extremity and tenderness in the left femoral triangle with a positive Homans' sign were noted. Dorsalis pedis pulsations were again absent, but femoral, popliteal and posterior tibial pulses were present. The patient was again placed at bed-rest and given anticoagulants. Moist heat was applied to the left thigh. Pain appeared to be subsiding but on the seventh hospital day, at approximately 10 a.m., the patient suddenly developed severe pain in the left thigh which required morphine for relief. Within an hour the left leg was deeply cyanotic from the toes to the inguinal ligament, and greatly increased in size. Measurements

of the legs revealed the left thigh to be 10 cm. larger than the right. Pulsations in the posterior tibial arteries were present and oscillometric readings of the ankle and foot were within normal limits. Both feet were cold, but the legs were warm. The left leg was "turgid" and deep blue in color. Pulsation of the left femoral artery appeared to be slightly diminished. There was no clinical evidence of shock. At the time of the acute episode the prothrombin time was 40 per cent of normal. The patient was unable to move his foot or leg because of severe pain. Pain was intense following passive motion.

The leg was immediately elevated to a 65° to 70° angle, and passive exercise, consisting of continuous flexion of the ankle, knee and thigh, with occasional rest periods, was started. Subcutaneous hexamethonium (2 c.c., 50 mg., twice daily) and oral dibenzyline (20 mg. twice daily) were begun soon after exercise was started. There was intense pain after any activity, and morphine sulfate was required during the period of exercise. Clotting time, by the Lee-White method, was maintained at

TABLE I

Oscillometric and Skin Temperature Determinations before and after 50 Mg. of Hexamethonium Subcutaneously

Oscillometric Readings

		Before	After
Right:	Foot	$\frac{1}{4}$	$1\frac{1}{2}$
	Ankle	3	$2\frac{1}{2}$
Left:	Foot	$\frac{1}{4}$	$1\frac{1}{2}$
	Ankle	$2\frac{1}{2}$	$3\frac{1}{2}$

Skin Temperatures *

		Before	After
Right:	1st Toe	20.0° C.	31.8° C.
	3rd Toe	20.0	31.4
	5th Toe	21.2	31.6
	Plantar Surface	24.6	31.8
Left:	1st Toe	20.2	31.5
	3rd Toe	20.4	31.4
	5th Toe	21.4	31.6
	Plantar Surface	25.0	32.0

* Room temperature, 22.0° C.

20 minutes by means of intravenous heparin. After four hours, active exercise was begun and continued for 36 hours. Cyanosis gradually disappeared in eight to 10 hours. Turgidity and swelling had subsided considerably after 20 to 24 hours. The leg was tightly wrapped after the third day. Three days after the acute episode, the left thigh was 8 cm. larger than the right. The color of the leg was normal and, with the exception of minimal pain in the left inguinal area, the patient was asymptomatic. Numerous superficial veins were noted over the left patellar and hip regions. The feet were cool, without evidence of gangrene or ulceration. Oscillometric readings and skin temperatures before and after injection of 2 c.c. of hexamethonium indicated that there was some evidence of abnormal vasoconstrictor tone present at rest in a cool room, but that this could be released by sympathetic blockade. There was no difference in the response in the right and left foot and no evidence to suggest definite organic arterial disease. (See table 1.)

The patient was ambulated on the seventeenth day with tight elastic support and, with the exception of slight residual edema, he remained asymptomatic.



FIG. 1. Phlebogram performed three weeks after acute episode.

A phlebogram done three weeks after the acute episode revealed no filling of the saphenous, deep femoral or iliac veins. A straight segment of a partially occluded vein in the midportion of the thigh was thought to represent a remnant of the superficial femoral vein. Numerous small collateral veins were visualized (figures 1 and 2).

The patient has remained on anticoagulant therapy and three months after the acute episode is asymptomatic except for occasional "tiring" of the leg. Superficial veins are no longer dilated and, with the exception of slight ankle edema when elastic support is not used, there are no abnormal physical findings.

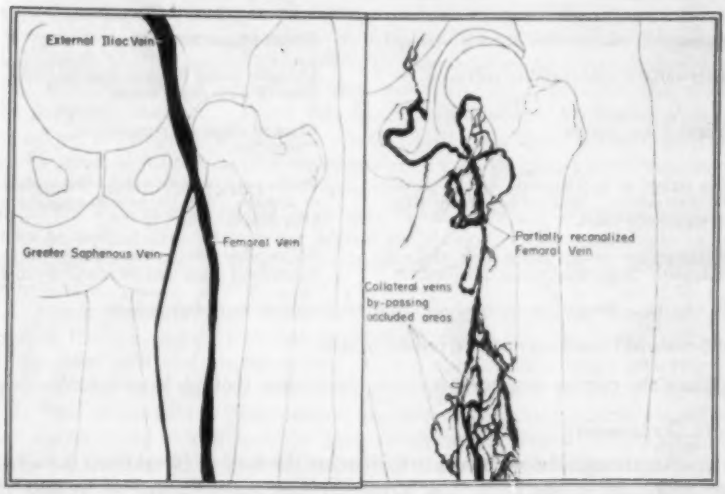


FIG. 2. Tracing of normal phlebogram, left leg, as compared to tracing of phlebogram in figure 1. Note absence of greater saphenous vein, and femoral and iliac veins. Numerous collateral veins have by-passed occluded segments. Partially recanalized femoral vein is noted.

DISCUSSION

1. *Diagnosis:*

Because of the marked difference in therapy in acute massive venous occlusion as opposed to acute arterial occlusion, it is extremely important to make a correct diagnosis. This may be especially difficult in elderly patients, because there may be coincidental obliterative arterial disease at the time of the venous occlusion. Peripheral pulses may be absent and yet not be associated with acute arterial blockage. Extreme difficulty in making the differential diagnosis may also be encountered because of a rather sudden vasoconstriction of the arterial vessels as well as the venous channels following an acute venous occlusion. This, too, may cause the peripheral pulses to be feeble or the oscillometric indices to be reduced. In arterial occlusion these latter findings are, of course, more pronounced.

There are two clinical signs of acute massive venous occlusion which should definitely suggest the diagnosis: (a) intense bluish-purple (cyanotic) discoloration of the extremity distal to the area of occlusion, and (b) marked edema and "turgidity" of the extremity. This often develops within a matter of minutes or hours. In contrast to this, in acute arterial occlusion the extremity is waxy or yellow-white and usually not markedly edematous. Other useful aids in making the correct diagnosis are listed in table 2.

TABLE II

Differential Diagnosis of Acute Arterial Versus Acute Venous Occlusion

Acute Arterial Occlusion	Acute Venous Occlusion
1. Extremity—wax-yellow in color.	Bluish-purple, cyanotic.
2. Extremity is cold distal to occlusion.	Extreme distal portion may be cold. Rest of limb often warm.
3. Slight if any edema	Marked edema, "congestion," "turgidity."
4. No pulses or oscillometric indices distal to obstruction. Will not be present after sympathetic block.	Pulses may or may not be diminished or absent. Will increase in amplitude after block.
5. Subpapillary venous filling time markedly delayed. Superficial veins collapsed.	Subpapillary filling time normal or rapid Superficial veins may be markedly dilated
Pain may be sudden or severe in both. May be unable to move feet in both.	
Numbness and paresthesias may be present in both.	

Once the correct diagnosis is made, immediate therapy is indicated.

II. *Treatment:*

A. An attempt should be made to increase the flow of blood from the affected extremity. Most observers now agree that the major pathology results from a complete blockage of "venous outflow" and an actual "damming up" of blood in the extremity.[2, 3, 4, 5] The role of associated arterial vasoconstriction ("vasospasm") is probably a secondary one.[2, 3] One would not expect that sympathetic blocks or sympathectomy, which would serve to release vessel tone and increase arterial inflow, would greatly or uniformly benefit the condition if nothing else were done. Actually, in some cases, patients have become worse, with the leg becoming increasingly more "swollen" as more blood flows in and is "trapped."[3] Similarly, since there is already a serious block of the venous system, ligation of the larger veins proximal to the affected area would not be expected to remedy the problem. The danger of embolization might present the only reason for ligation.

The method of increasing venous outflow has recently been well presented by Veal,[4] and consists of:

1. Immediate marked elevation of the extremity (65° to 70° angle).
2. Immediate passive and then active exercise of the extremity.

This latter method of therapy for venous occlusion appears to be the most effective way to produce a muscle "massaging and pumping effect" and increase flow in some of the collateral venous channels where the flow of blood has

virtually stopped. If flow can be reëstablished, stasis in the capillary and arteriolar segments, with resultant anoxia of the tissues and gangrene, might be prevented. The danger of "shock" can also be minimized in this manner, since severe shock may occur if sufficient quantities of blood become "pooled" in the extremity.[5, 6] Venous return to the heart must be maintained to avoid this serious complication.

B. Once some degree of flow is reëstablished, measures to release venous and arterial tone (relieve "vasospasm") may be instituted to produce the maximal flow to the part. This has previously been accomplished by the use of surgical blocking procedures or sympathectomy.[2-9] It has recently been demonstrated that chemical blockade of the sympathetic system with hexamethonium (C-6) produces as great an increase in peripheral blood flow as do the surgical procedures.[11, 12] The use of intravenous or subcutaneous hexamethonium would appear to offer definite advantages over surgical treatment, since the desired effect is rapidly obtained. When this agent is combined or alternated with oral dibenzyline, a sympathetic blocking agent which effectively releases arteriolar tone,[13] a continuous release of sympathetic tone can be achieved and maintained for as long a period as necessary. There is little danger in the use of these drugs in a patient who is kept in bed in a head-down position. With the release of venous as well as arterial tone for a sustained period of time, collateral venous channels are established. Heat to the abdomen will also aid in producing reflex vasodilatation.

C. Other measures that should be taken are: (1) the institution of anticoagulant therapy, and (2) the administration of sufficient analgesics and sedatives to allay pain and apprehension. (This may require large quantities of morphine, since pain is often excruciating during the early period of exercise.)

D. After the swelling, discoloration and severe pain have partially subsided, active exercise and elevation of the part should be continued. Firm wrapping of the entire extremity with elastic bandages should be employed even while the patient is in bed. This will aid further in promoting venous return. After ambulation, the patient should be fitted with an elastic stocking which should be worn continuously. He should also be instructed to sleep with the foot of the bed elevated from 6 to 10 inches. Management should be similar to that employed in any case of chronic venous insufficiency. Collateral channels will develop, as demonstrated in our case, but the major veins may remain occluded for many years and never again recanalize to an extent which will permit a significant flow of blood through them.

The success obtained in the cases of acute massive venous occlusion treated with exercise by Veal and in the one described above would seem to suggest that gangrene does not necessarily have to result following this catastrophe. The syndrome need not be entitled "venous occlusion with gangrene" if proper prompt therapy is instituted.

The number of patients treated in the above manner is small and many more cases will have to be treated successfully with exercise before this treatment will be established as the "method of choice." It would appear, however, that this therapy, based on the pathophysiologic findings in the entity, is the logical one to employ. Thus far, no evidence of dislodging of the clot by exercise or of pulmonary embolization has been obtained in the patients treated by

exercise (a total of 10). Again, the number of patients is too small to warrant the conclusion that there is no fear of embolization when this treatment is used.

Summary

1. A case of acute massive venous occlusion of a lower extremity is presented. This apparently resulted from extension of a previous thrombophlebitis.

2. Immediate treatment with elevation and continuous exercise of the extremity was employed, with excellent results. This treatment would appear to be the logical one to employ, since the major pathology in the condition results from "complete blockage" of venous outflow from the extremity. Efforts to promote this "outflow" should be made immediately.

3. Chemical sympathetic blocking procedures (oral dibenzyline and parenteral hexamethonium) were employed after exercise had been instituted. The use of drugs to produce release of reflex vasoconstriction would appear to present a definite advantage over the use of surgical procedures, especially in a patient who is on anticoagulant therapy.

Addendum

Since this paper was submitted for publication, we have had the opportunity to treat another patient with "acute massive venous occlusion" using the method described above with excellent results.

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CONGENITAL SYPHILIS OF THE STOMACH *

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TERTIARY syphilis of the stomach has always been a rather uncommon finding. Estimates of incidence vary from 0.1 per cent of syphilitic patients (Chase, quoted by Eusterman) to 4 per cent of gastric resections (Ayoma).[3] Eusterman in 1931 [1] reported 93 cases. Harris and Youmans [2] suggested that the following points should be met to provide a reasonably conclusive diagnosis of syphilis: (1) evidence of organic disease of the stomach, which on x-ray examination is indistinguishable from carcinoma; (2) a comparatively young individual; (3) the presence of other evidence of syphilis; (4) a qualified improvement under antisyphilitic treatment; (5) in cases operated upon, demonstrations of tissue changes compatible with syphilis.

Harris and Youmans reported seven cases, five males and two females. They state that when the syphilitic lesion is located near the pylorus, obstruction may be worse following antisyphilitic treatment and may require surgical intervention. Many of Eusterman's cases showed diminished gastric capacity and varying degrees of starvation. Epigastric pain or discomfort occurred soon after meals, unrelieved by food or alkali. In about a fifth of the cases the symptoms simulated peptic ulcer.

Clinical history is not helpful in recognition of gastric syphilis. In this condition the average age is lower than the average age in carcinoma of the stomach. Interval between the primary lesion and the diagnosis of gastric syphilis varies between 10 months and 25 years or more (Bockus).[3] Usually there is no evidence of syphilitic invasion of other systems in cases of proved gastric syphilis.

Bockus comments on the rarity of achlorhydria in active peptic ulcer, and its frequent association with gastric syphilis. The association of achlorhydria and carcinoma of the stomach must be borne in mind. Bockus and Bank [3] reported a death following perforation of the stomach during antiluetic therapy. Histamine-fast achlorhydria may, after antisyphilitic treatment, return to normal chlorhydric values.

Congenital syphilis of the stomach is a very uncommon condition. We have been able to find references to only two cases.

Verbrycke [4] reported a boy, seen by him at the age of 13 years. The child presented with complaints of epigastric pain and vomiting. At the age of 12 years he had had an uncomfortable, "full" feeling in the epigastrium, as if he had eaten too much. Relief of epigastric discomfort followed vomiting. Weight loss was considerable. For these complaints he had had an appendectomy, without benefit, and following x-rays, had been considered to have peptic ulcer by other physicians and surgeons.

None of the stigmata of congenital syphilis was present. Free hydrochloric acid was present in the gastric contents. Roentgenologically "the stomach was of a peculiar boot-shape, of fair tone, with slight increase in size of the fundus extending to nearly the distal third. Here the shadow became very narrow producing almost an hour-glass picture."

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Because it was thought that the gastric deformity could be due to nothing but syphilis without his general condition being much worse, syphilis was suspected, and the Wassermann was found positive. Under specific anti-syphilitic treatment rapid symptomatic recovery took place, and the child gained 24 pounds in one year. At the end of one year fluoroscopic examination showed a "distinctly favorable" change in gastric outline, but some narrowing of the antrum remained.

Marcus [5] reported the case of a 19 year old male who presented with complaints of upper abdominal distress and vomiting. Duration of complaints was approximately one year, with exacerbation in the previous three weeks. There was no pain but a sensation of fullness of the stomach, relieved by vomiting. Weakness had gradually increased, and there was some weight loss. No physical signs of congenital syphilis were noted. There was no free hydrochloric acid in the gastric contents. Fluoroscopy showed practically no food passing through the pylorus. A "colloid like tumor" occupying the pyloric end of the stomach was found at operation; it was resected, and gastroenterostomy was done. The histologic sections showed diffuse inflammatory lesions, considered to correspond to the picture of syphilitic inflammation. The patient died during postoperative convalescence; autopsy showed "syphilis of the stomach, myocardium, liver and kidneys; with focal arteriolar nephrosclerosis, acute peritonitis and purulent infarcts in the lungs."

No mention is made of spirochetal search of the tissues or of Wassermann reaction. Unfortunately, Marcus provides no data supporting the congenital origin of the syphilis, either by Wassermann tests of the parents or siblings, or by x-ray studies of the bones, etc. Accepting the diagnosis of syphilis on the histologic evidence, the presumptive congenital origin rests solely on the youth of the patient.

The following case of congenital syphilis, with gastric disease, is of interest.

Case Report

A white male, aged 20 years, was admitted on October 19, 1939, to the Western Division of the Montreal General Hospital with the complaints of vomiting following meals for four years, lower abdominal pain for four years, constipation for several years, tiredness and weakness, and loss of weight.

Present Illness: The patient had been well until four years before. Until then he had been able to play at such games as hockey, although he was always thin. About four years before admission he began to have crampy pains in the lower half of the abdomen following meals. The pain made him double up; doubling up his body or lying on his abdomen gave relief in a few minutes. Vomiting always followed soon after the pain, usually five to 10 minutes following the meal. Vomiting sometimes occurred without pain. He obtained some degree of relief by vomiting. The attacks were said to have occurred every summer since 1935, usually beginning about May and disappearing about the end of September. The current attack persisted longer than others.

He attended the M. G. H. Clinic in October, 1935, and was put on a diet and Sippy powders. With this his symptoms cleared. He did not return until September, 1939, when he presented with the above complaints. Recently he had been unable to retain the Sippy powders, as he vomited them. He had had no desire to eat.

Personal History: He was one of three children. He was born in Montreal and had always lived there. He had reached the sixth grade in school but had stopped



FIG. 1. Showing the Hutchinson's teeth.



FIG. 2. Showing the saber shins.

because of trouble with his eyes. Under the care of a physician he wore dark glasses for two years. His eye trouble had begun at about the age of 15. His recent occupation was that of carter in the city street cleaning department. He was said to have had rickets in childhood. There was no history of any other illness. He denied ever having had any sexual exposure. The father, age 47, was alive and well. The mother, 30, was alive and well. Her Wassermann test (1939) was negative. She had had no miscarriages. The patient had one brother and one sister, both alive and well. He had never had tarry or bloody stools. He had not had jaundice. At the age of 16 years he had weighed 95 pounds; on admission (age 20) he weighed 84 pounds.

Physical Examination: The body was emaciated and the color sallow. There were no opacities of the lens or cornea. The ears were normal; there was no discharge and no deafness. Hutchinson's teeth were present. There was slight en-



FIG. 3. (1939) The stomach presents a large filling defect, producing an hour-glass constriction; peristalsis was not observed in this portion, but was seen in the parts of the stomach on each side of the filling defect.

largement of the inguinal lymph nodes. The epitrochlear lymph nodes were not palpable. Pulse was 66 and regular; blood pressure was 90/78 mm. of Hg. The heart was not enlarged, and there were no murmurs. Examination of the abdomen was negative. Cranial nerve system was negative. The tibiae showed pronounced anterior bowing (saber shins). Mental development seemed about normal. Testicles were normal to physical examination. Emaciation of the body was striking. The joints were normal.

Special Examinations: There was no free hydrochloric acid in the stomach. There was no blood in the stools. Blood Wassermann test was positive. Spinal fluid was negative. Urinalysis was negative. Hemogram was normal. Blood sugar was 105. X-ray of the skull was negative; there were no changes in the pituitary fossa. Retinoscopy showed retinitis of the "salt-and-pepper" type, compatible with the diagnosis of luetic retinitis. On gastroscopy, on the greater curvature about the



FIG. 4. Six-hour gastric barium retention is shown, and a barium rest on the posterior wall, near the greater curvature.

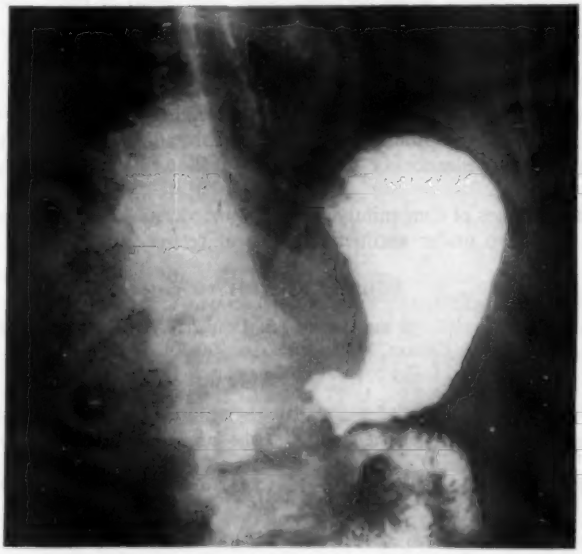


FIG. 5. Stomach (May, 1953), showing normal contour and normal function.

site of the barium rest seen in the x-ray, was an ulcer with a dirty green base, with no sign of healing or granulation on the margins. The instrument could not be advanced into the lower half of the stomach. The mucosa of the upper half showed considerable superficial gastritis, as evidenced by the reddened, swollen folds, small and aberrant in distribution, which did not flatten out on inflation. The achlorhydria was carefully investigated. Under fluoroscopic control it was shown that no free hydrochloric acid was present in either segment of the stomach; the achlorhydria was absolute to alcohol and histamine. Combined fluoroscopic and serial x-ray film examination of the gastrointestinal tract showed an absence of the mucosal markings. In the spot film taken in the upright position there was a rounded collection of barium on the posterior surface of the stomach towards the greater curvature. There was a barium "rest" at six hours in this region. There was a filling defect involving the pars media. At six hours the stomach was not completely emptied.

Treatment consisted solely of antiluetic measures. Iodides and bismuth were given at first, later arsenic (Novarsenobenzol). Remission of symptoms was rapid. Vomiting ceased, and strength and nutrition improved rapidly. From admission on October 19 until discharge on December 2, the weight increased from 84 to 92½ pounds. Following hospital discharge the patient received regular treatment for syphilis in the out-patient department.

He was recalled for examination in April, 1953. He had developed into a healthy looking man, and had had no illness since terminating the antiluetic treatment. He had been employed in various jobs, chiefly in general labor and as a chauffeur. He was unmarried. He now weighed 134 pounds. His teeth had been extracted because of caries, and he used dental plates. The saber shins and the scars of the retinitis were the only remaining signs of the congenital syphilis. Abundant free hydrochloric acid was present. Fluoroscopic gastric examination showed disappearance of the lesions previously described, and completely normal appearance and function. No abnormality of the nervous system, skin, heart or lungs was seen.

Summary

The symptomatology of gastric syphilis is reviewed.

A case of congenital syphilis of the stomach is reported, with 14 year follow-up.

Disappearance of symptoms, return to normal radiologic appearance of the stomach, and disappearance of achlorhydria followed treatment by iodides, bismuth and arsenic.

Of the three cases of congenital syphilis reported, one operated upon (gastric resection) died, two under antiluetic treatment recovered.

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EDITORIAL

VITAMIN B_{12} AND MEGALOBLASTIC ANEMIA: RECENT STUDIES

SINCE 1948 three substances have been available to the clinician for the treatment of megaloblastic anemias. These three, all members of the vitamin B complex, are folic acid, citrovorum factor (folinic acid), and vitamin B_{12} (cyanocobalamin). Studies of their interrelationship have not only cast new light on the pathogenesis of pernicious anemia, but also permit further insight into the complexities of nucleoprotein metabolism. Although much remains to be elucidated, a brief resumé of some significant recent contributions may be of interest.

With the exception of rare cases of refractory megaloblastic anemia (achrestic anemia) all other megaloblastic anemias respond favorably, either permanently or in transient fashion, to folic acid or its derivative, folinic acid. It is now quite clear that the response of pernicious anemia to folic acid is of a temporary nature and that hematologic relapse will occur despite continued therapy. Moreover, the progression of neurologic damage, despite hematologic remission, during such therapy is of even graver consequence.[1] Conversely, the failure of liver extract or vitamin B_{12} to cure the megaloblastic anemias of pregnancy and infancy has been well documented.[2, 3] Thus, despite certain apparent similarities of these entities subtle differences in pathogenesis exist.

Folic acid and vitamin B_{12} are both involved in the maturation of megaloblasts. Much of the information regarding their metabolic action is derived from microbiological studies. Both are concerned with nucleoprotein metabolism[4]—folic acid with the formation of purines and thymine from simpler precursors, and vitamin B_{12} with the formation of nucleosides (thymidine) from the purines and pyrimidines. From thymidine are formed nucleotides and hence nucleic acid. Carrying over these bacteriologic studies into clinical hematology, one might say that the primary biochemical defect in pernicious anemia is an inability to synthesize certain nucleosides, particularly thymidine, from parent purines or pyrimidines. The ineffectiveness of vitamin B_{12} in certain megaloblastic anemias may be due, therefore, to the breakdown of earlier links in the chain which are under the influence of folic and folinic acid. On the other hand, the latter, by mass action, are able, temporarily at least, to overcome a deficiency of vitamin B_{12} such as exists in pernicious anemia. Other megaloblastic anemias (megaloblastic anemias of pregnancy and infancy, the sprue syndrome,

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tropical macrocytic anemia, etc.) are most likely folic acid deficiencies from the outset and are therefore entirely susceptible to the action of this vitamin alone. These basic facts, as important as they are, do not portray the complete pathogenetic mechanisms which operate in megaloblastic anemias.

The availability of substances of known composition since the synthesis of folic acid in 1945 and the isolation of vitamin B_{12} in 1948 have permitted important amplification and modification of Castle's hypothesis of the pathogenesis of pernicious anemia. It is now generally accepted that vitamin B_{12} is Castle's extrinsic factor.[5] Its main source in nature is the synthetic activity of various microörganisms, especially bacteria of the streptomyces group.[6] Herbivorous animals obtain vitamin B_{12} from the microflora of their digestive tracts rather than from higher plants and store it in various tissues. Vitamin B_{12}-like activity has been found in the feces of normal humans as well as patients with pernicious anemia in relapse. Although it is not certain whether this is of alimentary or bacterial origin, there is some evidence that it may be synthesized in the colon in man.[7] Chemical studies have shown that vitamin B_{12} is a cyano-cobalt coördination complex. Brink et al.[8] suggested the name Cobalamin for that part of the molecule attached to the cyano group. Several chemical forms have been found. Vitamin B_{12} is cyanocobalamin, B_{12b} hydroxocobalamin, B_{12c} nitroso-cobalamin.[9] The various forms differ somewhat in microbiologic activity, but not in clinical activity.[10, 11] They can all be converted to vitamin B_{12} by the addition of sodium cyanide to the assay medium. The vitamin B_{12} activity of various substances is determined microbiologically by their effect on the growth of suitable organisms, notably *Lactobacillus lactis Dorner*, *Lactobacillus leichmannii*, and *Euglena gracilis*. These technics are now extensively employed for the assay of commercial preparations of the vitamin.[12]

The nature of the intrinsic factor of Castle still defies complete identification although important recent advances in knowledge have occurred. Latner et al.[13] employing the technic of filter paper electrophoresis of con-

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centrated normal gastric juice have isolated several fractions with intrinsic factor activity. The more potent of these appears to be a mucoprotein or mucopolysaccharide. Glass and his co-workers [14] also believe that glandular mucoprotein, a heterogeneous complex of mucin derived from the fundal glands and corpus of the stomach, is the intrinsic factor. In 1949, Ternberg and Eakin [15] isolated a heat-labile, non-dialyzable fraction from normal gastric juice which they termed apoerythrein and which had the important property of combining with vitamin B_{12} and rendering it microbiologically inactive. This complex can be dissociated by heat, enzymatic digestion, or autolysis with liberation of the cyanocobalamin for microbiological activity. As a result of these studies they suggested that the physiologic function of intrinsic factor is to bind vitamin B_{12} and render it immune to the action of intestinal bacteria. Although this may be an important aspect of intrinsic factor activity it is not the entire story. Prusoff et al.[16] in studying various fractions derived from desiccated hog stomach found that those fractions most effective for vitamin B_{12} binding were less effective in potentiating the vitamin, i.e., in intrinsic factor activity.

It seems most likely that the important physiologic function of intrinsic factor is directly and specifically to facilitate the absorption of cyanocobalamin by the intestinal wall. The oral administration of small doses (5 micrograms) of vitamin B_{12} is hematopoietically ineffective unless a source of intrinsic factor is simultaneously administered. In this connection it is of interest to note that the favorable results obtained by Minot and Murphy in their early liver feeding experiments were probably due to the folic or folinic acid content of the liver. These vitamins do not require intrinsic factor for absorption across the intestinal barrier. On the other hand, the liver extracts given parenterally a few years later were effective as a result of their vitamin B_{12} content. Commercial liver extract contains very little folic acid.

Recently Heinle et al.[17] have shed additional light on the action of intrinsic factor by the use of radioactive cobalt labelled vitamin B_{12}. The administration of 0.5 microgram doses of labelled cyanocobalamin by mouth to patients with pernicious anemia, in relapse or remission, resulted in the excretion of 70 to 95 per cent of the dose in the feces. The simultaneous administration of gastric juice or hog stomach concentrate reduced the excretion to 5 to 30 per cent. The importance of this technic lies not only in its clarification of the action of intrinsic factor, but also in the fact that

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it affords a method for the diagnosis of pernicious anemia in a patient in complete remission. The facilitation of absorption by intrinsic factor is a transient phenomenon. When intrinsic factor is administered four hours before an oral dose of vitamin B_{12} a hematologic response will occur. If the interval between the two is 12 hours or more no hematologic response occurs.[18] Ungley [19] has suggested that intrinsic factor catalyzes some enzyme process in the intestinal epithelium which is directly concerned with the absorption of vitamin B_{12}. Oral doses of cyanocobalamin of considerable magnitude (3000 micrograms) without intrinsic factor will produce the hematopoietic effect of 20 to 40 micrograms given parenterally.[20]

Employing the technic of microbiologic assay, Mollin and Ross [21] demonstrated that parenterally injected vitamin B_{12} circulates in a microbiologically active form, i.e. unbound, for about eight hours during which time a considerable portion is excreted in the urine; after this time it becomes bound and very little urinary excretion occurs. Reisner and Weiner [22] noted that when large (100 to 1000 micrograms) doses of vitamin B_{12} are administered parenterally, 51 to 98 per cent of the injected dose is excreted in the urine. Sokoloff et al.[23] found that at a dosage level of 42.2 micrograms parenterally, very little urinary excretion occurs. The binding of cyanocobalamin seems to proceed at a constant rate. When blood levels are raised, free vitamin B_{12} is eliminated in larger amounts. These data are of great significance with regard to the current suggested clinical usage of massive doses of vitamin B_{12} in the treatment of various types of neuropathies. The nature of the binding process will be discussed further below.

Bone marrow cultures in vitro have recently yielded important information. Lajtha [24] demonstrated that normal bone marrow when cultured in the serum of a patient with pernicious anemia in relapse showed conversion of normoblasts to megaloblasts. Pernicious anemia serum appeared to contain an inhibitor of megaloblast maturation. Megaloblastic marrow cultured in mixtures of varying concentrations of normal and pernicious anemia serum revealed that the inhibitor could be overcome by increasing the concentration of normal serum. The inhibitor was thermostable and could also be demonstrated in the cerebrospinal fluid of pernicious anemia patients in relapse. The addition of folic acid and folinic acid to megaloblastic marrows cultured in pernicious anemia serum resulted in maturation

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of the megaloblasts. Vitamin B_{12} had no such effect. However, the addition of vitamin B_{12} combined with a thermolabile substance from gastric juice was effective in producing megaloblast ripening. The B_{12}-intrinsic factor complex was microbiologically inactive. Heating disrupted the complex and rendered the vitamin available to the test organism, but incapable of maturing megaloblasts.

It seems paradoxical that free cyanocobalamin administered intramuscularly should be clinically effective and yet in vitro incapable of causing megaloblast maturation. Apparently only when bound is it hematopoietically active. The nature of the binding material and its source are at the moment unsettled. Callender and Lajtha [25] have suggested that there is an extra-gastric type of intrinsic factor with which vitamin B_{12} combines. Mollin and Ross found a close correlation between the level of bound vitamin and the state of maturation of red cell precursors in the marrow during the treatment of pernicious anemia.

These and other studies have resulted in a re-awakening of interest in the toxic and hemolytic aspects of pernicious anemia. Recent studies indicate that during relapse there is definitely accelerated destruction of the patient's own cells as well as tagged normal cells given by transfusion. This phenomenon disappears during remission.[26]

Despite many gaps which remain to be filled by further experimentation, Callender and Lajtha offer the following hypothesis for the action of folic acid, folinic acid, and vitamin B_{12} in megaloblastic anemias. Both cyanocobalamin and folic acid are necessary for normal hematopoiesis and one is ineffective in the total absence of the other. Virtually all megaloblastic anemias will respond, at least temporarily, to folic or folinic acid. Some are true folic acid deficiencies and will respond only to folic acid. The partial effectiveness of folic acid in pernicious anemia is due to mass action. In the untreated pernicious anemia patient the action of dietary folic acid on hematopoietic cells is blocked by an inhibitor in the serum. Vitamin B_{12} plus gastric intrinsic factor given orally or plus extra gastric intrinsic factor when given parenterally, forms a "hematopoietic factor" which counteracts the action of inhibitor either directly or indirectly on the red cells. Either "hematopoietic factor" or vitamin B_{12} is concerned with the normal function of the central nervous system.

In conclusion, several points of immediate clinical interest may be mentioned. The time seems close at hand when a potent source of intrinsic factor combined with vitamin B_{12} may provide a satisfactory oral method of treatment of pernicious anemia. Several problems remain to be solved by careful clinical observation. Because of the variability of absorption of a given amount of cyanocobalamin the proper ratio of intrinsic factor to

[25] Callender, S. T., and Lajtha, L. G.: On the nature of Castle's hematopoietic factor, Blood **6**: 1234, 1951.

[26] De Gorvin, E. L., Hamilton, H. E., Sheets, R. F., Jauney, C. D., and Ellis, J. A.: The role of maturation arrest in the low erythrocyte counts of pernicious anemia, J. Lab. and Clin. Med. **40**: 790, 1952.

vitamin must be meticulously worked out. Another variable to be overcome is the problem of differences in the recipients of the medication.

A number of recent studies [27, 28, 29] offer sufficient clinical evidence to warrant further study of the value of vitamin B_{12} in the treatment of painful, peripheral neuropathies of diabetic, nutritional and other origin. The mode of action is as yet obscure but may be related to the influence of vitamin B_{12} on ribose nucleic acid synthesis in nervous tissue.

MILTON S. SACKS, M.D.

[27] Saucetta, S. M., Ayres, P. R., and Scott, R. W.: The use of vitamin B_{12} in the management of the neurologic manifestations of diabetes mellitus, with notes on the administration of massive doses, Ann. Int. Med. **35**: 1028, 1951.

[28] Bean, W. B., Franklin, M., and Saks, A. L.: An effect of vitamin B_{12} on pain in nutritional neuropathy, Am. J. M. Sc. **220**: 431, 1950.

[29] Levy, I.: The use of vitamin B_{12} in the symptomatic treatment of peripheral neuropathy—a preliminary report, Trans. Am. Neurol. As. **267**, 1950.

REVIEWS

Klinische Fehldiagnosen. By Prof. Dr. M. Bürger. 481 pages; 17.5 × 24.5 cm. Georg Thieme Verlag, Stuttgart; agents for U. S. A.: Grune & Stratton, Inc., New York. 1953. Price, Ganzleinen DM 58.50.

Bürger undertakes to contrast clinical impressions against diagnoses established by the direct examination of structures by the pathologist or surgeon. He attacks the important art of differential diagnosis by throwing into relief the commonest mistakes in interpretation of the symptoms and signs offered by diseases in each organ system.

The author first discusses the limitations of the various procedures, including physical examination and not neglecting intuition, leading to clinical impressions. He discusses the fallibility of supposedly purely objective criteria offered by the laboratory. "Negative" tests in the face of patent disease must be repeated or discarded. The occasional "positive" test contradicting other findings must be regarded with a jaundiced eye. Like all good clinicians he gives the history first importance. Many patients bring a list of confusing diagnostic errors from their former medical attendants. It is the nature of certain patients and certain illnesses to falsify or color certain manifestations or intentionally omit pertinent facts. He emphasizes that we deal with sick people rather than with sicknesses. Clinical medicine is the study of the pathological physiology of the person.

Separate chapters deal with the commoner mistakes in diseases of various organs and organ systems: the lungs, the mediastinum, the parts of the gastrointestinal tract, the heart and arteries, the spleen, lymph glands, the kidneys, the nervous system, metabolism, infections and occupational diseases. The earlier chapters are much more detailed than the closing chapters.

Bürger defines dysgnosis as viewing one finding or condition disproportionately, as occupying one's self with cardiac infarction when some condition such as cancer makes surgery inevitable. Dysgnosis also is incorrectly evaluating correct findings.

Agnosis is defined as intentionally discarding diagnostic findings. He mentions Hahnemann who paid no attention to anatomy or physiology. A doctor may be so oblivious to the severity of his patient's illness or approaching death as to persist in dangerous or disturbing diagnostic procedures. Diagnostic or therapeutic nihilism are to be avoided; it is preferable to do too much rather than too little. Essential to the diagnosis is the distinction between a temporary disturbance of physiology or a permanent disturbance like Hodgkin's disease, chronic nephritis or cirrhosis of the liver.

Bürger would have norms established for each age group before calling conditions abnormal. Important to him is a satisfactory delineation of gerontology with its colorings of disease and its implications in diagnosis.

Diagnoses made late amount to mistakes leading to therapeutic failures avoidable by a prompt diagnosis in such conditions as pneumonia, tuberculosis and many kinds of cancer.

In this connection he advocates examination of the apparently healthy, particularly in industry to permit early finding of such conditions as aniline dye poisoning and the pneumonokonioses. The field of early disease, the borderline between health and sickness is most productive of diagnostic errors.

Continuing his stimulating discussion of industrial diseases originating in the flourishing chemical concerns making new cleaning materials, solvents, poisons for insects and rodents, plastic materials and oil products, he urges awareness of substances producing systemic disease as well as local irritation. The allergic individual, a possible industrial liability, is to be sought out and protected.

The discussion of plumbism is thorough. Small amounts of lead are so stimulating to the marrow as to produce stippling before other signs of plumbism are manifest—75 per cent of apparently healthy lead workers may show stippling. Interesting is the description of the cases of lead poisoning resulting from the melting down of metal from wrecked ships and from the bridges destroyed in World War II.

The description of pitfalls in the diagnosis of lung diseases is especially thorough. The subject of mediastinal tumor is well illustrated by numerous reproductions of chest films. He gives little consideration to sarcoidosis in his treatment of hilus changes.

Diseases of the circulation are exhaustively and differentially described. Especially good are the discussions of circulatory disturbances in sports and of "black cardiacs." His explanation of the Austin-Flint murmur is novel. The pathogenesis of arteriovenous aneurysms is detailed. He has given particular consideration to the finding of cardiac aneurysm. The arteritides are clearly differentiated by a chart.

Diseases characterized by splenomegaly are differentially described. The lymphomas are well considered. Infectious mononucleosis is not mentioned as such. American readers will hardly recognize it as "monocytic angina." He does not accord it its usual importance in discussing leukemia.

Bürger's clinical skill is well shown in his chapter on liver disease. The possible errors in recognizing infectious hepatitis are clearly portrayed. He makes a point of the differential value of comparing the nitrogen in the serum with the nitrogenous content of ascitic fluid. He attempts to differentiate infectious hepatitis from catarrhal jaundice.

He properly emphasizes the difficulties in recognizing and distinguishing diseases of the pancreas. The causes of hypoglycemic syndromes are delineated skillfully.

Porphyria is mentioned as a justifiable consideration in conditions resembling epilepsy especially those with digestive complaints.

Fever as a diagnostic problem receives rather brief consideration.

"Rheumatism" is well recognized as a waste basket of diagnostic errors. Starvation osteopathy is a described form of osteoporosis unknown to American readers. Bürger points out that small, miliary carcinomatous metastases to bone are very painful; a solitary large metastasis may be silent until announced by a pathological fracture.

Amidopyrin still apparently enjoys great favor in Europe although the American discovery of its neutropenic effect is finally recognized. "Focal infection" and its implications are still prominently discussed in Europe as contrasted with their markedly lessened importance in American literature. Increase in the incidence of peptic ulcer is attributed to decreased tissue resistance rather than to the psychic factors usually considered in this country.

Some of the x-ray reproductions show the lack of detail so usual in such attempts at illustration.

The author shows the usual German unfamiliarity with American literature. This may be due rather to inaccessibility of material than to intentional omission. Bürger has quoted some American authors, acknowledging the progress in American medicine during a concurrent period of stagnation in European medicine.

On the other hand, the author is obviously familiar with the best German medical literature.

In general the book bespeaks a vast clinical experience and thoughtful medical philosophy, sterling internist qualities.

This work may well accompany a renaissance in German medicine. It is a good argument for the resumption of the study of German by medical students desiring to supplement American information with the knowledge afforded by European medicine.

Any internist, especially those with consultation practices, could well review Bürger's book periodically.

EUGENE F. TRAUT, M.D., F.A.C.P.

The Management of Abdominal Operations. Edited by RODNEY MAINGOT, F.R.C.S. 1253 pages; 17 × 25.5 cm. The Macmillan Co., New York. 1953. Price, $24.00.

This single volume of 1253 pages consists of the contributions of 33 physicians and surgeons who have written 47 chapters edited by Rodney Maingot.

The volume deals with subjects all dedicated to safer surgery through good advisement as to the preoperative, operative and postoperative management of the patient. The contributors are all British surgeons and physicians but liberal references are made to American experiences.

Grading of patients as to cardiac, respiratory, urologic and nutritive status is discussed generally as well as specifically with each contemplated surgical procedure. General and specific preoperative management is handled in a similar manner. Ample space is reserved for the laboratory side of the various pictures. The problems of anesthesia, shock, the use of blood and substitutes, antibiotics, patient hydration and alimentary decompression are presented. The surgical affections of each organ of the gastrointestinal tract are individually discussed in detail. Postoperative complications and their management (particularly after gastric operations) are given excellent consideration.

Equivocal problems are attractively approached by the various authors. Pertinent and debatable questions are poised and frank opinions recorded concerning controversial subjects.

Altogether, this book represents an informative, well organized, attractively written modern text on the subject. It is felt that any surgeon or internist interested in the field of abdominal surgery could gainfully spend many hours with this volume.

H. C. H.

Hormonal Factors in Carbohydrate Metabolism. Volume VI, Ciba Foundation Colloquia on Endocrinology. General Editor for the Ciba Foundation: G. E. W. WOLSTENHOLME, O.B.E., M.A., M.B., B.Ch.; assisted by JESSIE S. FREEMAN, M.B., B.S., D.P.H. 350 pages; 14 × 21 cm. Little, Brown and Co., Boston. 1953. Price, $6.75.

The conference presented in this book was under the chairmanship of C. H. Best. C. F. Cori, F. D. W. Lukens, F. Verzar, J. W. Conn, J. A. Russell, D. R. Drury, R. D. Lawrence, I. A. Mirsky and other leaders in the field of carbohydrate metabolism contributed sections and participated in discussions. Anterior pituitary, adrenal-cortical, sex, pancreatic hyperglycemic and pancreatic hypoglycemic hormones were considered in their relationships to carbohydrate metabolism. Much of the data came from recently developed technics of isolated surviving tissue studies, compounds of radioactive carbon, hepatic vein catheterization and chromatographic separations.

Some of the conclusions of possible interest to clinicians follow:

Insulin appears to have a lipogenic action, to decrease the output of glucose from the liver, to stimulate uptake of glucose, deposition of glycogen and formation of CO_2 in muscle. Some insulin resistance is attributable to insulinase activity. The commonest type of diabetes in the middle-aged obese adult is the "lipoplethoric" type which involves increased insulin requirement. The diabetes occurring in younger people is typically of the "insulin deficiency" type. The complications of diabetic pregnancy are unlike preëclamptic toxemia. The fructose level of semen is related to the blood glucose level and to gonadotropic hormone.

G. E. G.

Office Psychiatry: The Management of the Emotionally and Mentally Disturbed Patient. By LOUIS MOENCH, Assistant Clinical Professor of Medicine and of Psychiatry, University of Utah School of Medicine. 310 pages; 21 × 14.5 cm. The Year Book Publishers, Inc., Chicago. 1952. Price, $6.00.

This book is written for physicians and medical students, not to make psychiatrists of them, but to increase their understanding of patients as persons, thereby extending the range of their usefulness to their patients, and adding to their own satisfaction. The material is from Dr. Moench's own wide experience in psychiatry, from his investigations of psychosomatic disorders, notably *headache*, and from the experience of others. It is presented in the form of explanatory and descriptive notes filling in a broad outline under 13 chapter headings, each chapter dealing with a particular aspect of office psychiatry. The text is illustrated with clever line drawings and brief summaries of case histories. Each chapter has its own bibliography, referred to by numbers in the text. Some controversial statements are not substantiated by reference to clinical data, but many of the references will lead the reader to articles or books which deal more fully with specific topics than can be dealt with in a survey book of this kind.

The six chapters (3 to 8) which make up the largest portion of the book adequately cover most of the psychiatric problems seen by the non-psychiatrist—psychosomatic medicine, neuroses and psychoses, with special attention given to the management of depressed and suicidal patients, and patients with toxic reactions. The latter chapters of the book on examination, interviewing and psychotherapy are more difficult to understand. The phraseology becomes technical without clear explanation of terminology; and major points are often obscurely made. The doctor-reader is advised to look at himself and his effect on his patients, and to ask more questions of himself than he asks of the patient. He is asked to perform differently in a psychiatric examination than he does in his usual office examination. To be able to do this, however, would require a certain perception toward which the physician is given little guidance in this book. It is scarcely mentioned that self-awareness is hard to achieve, and can best be attained by supervised training in interviewing technics. A disproportionate amount of space is given over to the discussion of psychological testing. Some readers may get the mistaken idea that a 20 minute paper-and-pencil test can hand the doctor a sure psychiatric diagnosis.

The need for such a book is great, and on the whole Dr. Moench has admirably achieved his purpose in writing the book. This is a book which many thoughtful physicians will find exceedingly helpful; but hurried doctors who seek a manual of psychiatric formulae will find it disappointing.

V. S.

Tumors of the Lower Respiratory Tract. (Atlas of Tumor Pathology, Section V, Fascicle 17.) By AVERILL A. LIEBOW, M.D., Professor of Pathology, Yale University School of Medicine. 189 pages; 20 × 26 cm. (paper-bound). Published by the Armed Forces Institute of Pathology, under the auspices of the Subcommittee on Oncology of the Committee on Pathology of the National Research Council, Washington, D. C. 1952. Price, $1.25.

This is another section comprising the Atlas of Tumor Pathology from the Armed Forces Institute of Pathology. These excellent monographs are evolving slowly in the form of loose leaf fascicles which, when completed, will represent the best pictorial and descriptive atlas on tumors in existence.

The Armed Forces Institute of Pathology, acting as the central registry with five other co-sponsors and supporters, is pursuing this herculean task.

This section by Dr. Liebow, Professor of Pathology at Yale, follows the usual pattern of short but pertinent descriptions and discussions of tumors in the lower respiratory tract. The gross and photomicrographic illustrations are prolific and excellent. In this 189 page fascicle there are 249 photographs, 10 in color. One hundred and seventy-five references show a wise and restrained use of the literature in amassing, classifying and presenting this wealth of material. The rare tumors are neither slighted nor emphasized. A limited section is devoted to the cytological examination of cells in sputum and pleural fluid. This is presented in the correct conservative fashion, as a possible diagnostic aid rather than as a short cut to diagnosis.

This is an excellent reference work; a must for the pathologist and teacher, valuable to the internist, chest surgeon and oncologist and of some little use to the practitioner.

C. G. W.

Clinical Electrocardiography: A Textbook for Practitioners and Students. By Dr. MAX HOLZMANN, Zurich; translated by DOUGLAS ROBERTSON, M.A., D.M. (Oxon), M.R.C.P. (London). 647 pages; 16 × 25.5 cm. Staples Press, London and New York. 1953. Price, $21.00.

This outstanding volume is the English translation of the second German edition of Dr. Holzmann's text on clinical electrocardiography. The author's attitude is a healthy one, "To the physician there can only be *clinical* electrocardiography, as its findings can be properly interpreted and exploited to the full only in their clinical context. . . . Its adoption by a large number of general practitioners has led to a tendency to regard the tracings as too unequivocal. Wrong diagnoses are often the result, and the method is apt to be discredited in the eyes of the uninitiated. Clinical electrocardiography, therefore, must obviate such erroneous ideas. . . . We have purposely avoided an over-simplified, schematic, and apparently clarified exposition of the subject, even though this may make things more intelligible and more acceptable to the beginner; but this would be scientific make-believe, and hinder progress. Such an attitude is part of the reason why electrocardiography has, in the past, been successively subject to over- and under-estimation."

The text goes far to fulfil the author's objectives. There is adequate and complete coverage of anatomical and electro-physiological principles. The section on the normal electrocardiogram (121 pages) discusses in detail the normal electrocardiogram and provides a sound basis for understanding the mechanisms and significance of departures from normal. The author refers repeatedly to vectorial principles in this section, and throughout the volume. There is a large section on the abnormal electrocardiogram other than disturbances of rhythm, and another devoted to disorders of rhythm, in addition to smaller sections on less important topics.

This book is unusual because of its fundamental approach and because of the completeness of the discussions in the text. The author recognizes that the development of the theoretical side of electrocardiography has not kept pace with the practical application of the method. The illustrations and diagrams are good, and the text is interestingly written, detailed, and informative. The section on congenital heart disease is too brief. The bibliography is generally good; but some of the more recent significant American papers are not referred to. A more complete index would add to the usefulness of this text.

Dr. Holzmann's new volume ranks among the best texts on electrocardiography, and is recommended to serious students of the subject, both new and experienced.

S. S.

The Physiologic Effects of Wounds: Surgery in World War II, Medical Department, United States Army. By the Board for the Study of the Severely Wounded, North African-Mediterranean Theater of Operations. 376 pages; 17.5 × 25.5 cm. Office of the Surgeon General, Department of the Army, Washington, D. C. 1952. Price, $3.50.

This book is the first in a series of 34 volumes on the history of the United States Army Medical Service in World War II. It has been published under the direction of the Surgeon General, Department of the Army. It is an excellent compilation of data obtained from battlefield experiences gathered by the Board for the Study of the Severely Wounded in the North African-Mediterranean Theater of Operations, World War II.

There is an excellent resumé, both statistically and clinically, of the condition of the severely wounded on hospital entry. Detailed studies were made on plasma protein concentration and hematocrit values. Comparative studies were also made in order to evaluate the rôle of plasma and of whole blood. Liver function studies were determined by means of bromsulphalein excretion, both from the viewpoint of trauma and also from the effects of ether anesthesia. It was noted that generally there was a sharp increase in bromsulphalein retention in patients deteriorating rapidly. Attempts at measuring renal function in order to correlate the effects on the severely wounded are also described. Excellent observations are included in reference to lower nephron nephrosis. Considerable detail is devoted to the description of clinical physiologic and the biochemic correlation, and their effects and changes in the severely wounded are included. The treatment of lower nephron nephrosis is described and there is an attempt at correlation of the various approaches to therapy. Types and quantities of fluid to be administered during the period when renal failure is most severe are discussed.

The rôle of alkalies in traumatic shock is discussed and very informative statistical information and observations are projected. There is an excellent chapter on the pathology of the kidney. Necropsy findings in 60 severely wounded casualties are included. The rôle of sulfonamides in relation to shock is described. It is believed by the authors of this book that the variation in the blood sulfonamide levels was too great in all categories studied to yield reliable correlation between blood level and renal insufficiency.

An extremely interesting chapter describes the crush syndrome in battle casualties. It describes the clinical features of the condition, physiologic and biochemic features as well as pathology and treatment. There is an excellent compilation of all cases included in this study. They were classified according to shock on admission, major wounds or injuries and their outcome. The book is extremely well indexed. It should make an excellent volume as a study text in this type of problem.

G. H. Y.

BOOKS RECEIVED

Books received during December are acknowledged in the following section. As far as practicable those of special interest will be selected for review later, but it is not possible to discuss all of them.

Advances in the Control of Zoonoses: Bovine Tuberculosis, Brucellosis, Leptospirosis, Q Fever, Rabies. WHO/FAO Seminar on Zoonoses, Vienna, November, 1952. World Health Organization: Monograph Series. 275 pages; 24 × 16 cm. (paperbound). 1953. Published jointly by FAO and WHO and issued also as FAO Agricultural Studies No. 25. World Health Organization, Geneva; available in U. S. A. from Columbia University Press, International Documents Service, New York. Price, $3.00.

Autopsy Diagnosis of Congenitally Malformed Hearts. By MAURICE LEV, M.D., Pathologist and Chief of Research Laboratories, Mount Sinai Hospital of Miami, Miami Beach, Florida, etc. 194 pages; 24.5 × 16 cm. 1953. Charles C. Thomas, Publisher, Springfield, Illinois. Price, $7.50.

Design and Operation of Septic Tanks: Third European Seminar for Sanitary Engineers, 27 October–1 November 1952, London, England. World Health Organization Monograph Series No. 18. 122 pages; 24 × 16 cm. 1953. World Health Organization, Geneva; available in U. S. A. from Columbia University Press, International Documents Service, New York. Price, $1.50.

Diagnosis of Acute Abdominal Pain. By WILLIAM REQUARTH, M.D., Clinical Assistant Professor of Surgery, University of Illinois College of Medicine. Foreword by WARREN H. COLE, M.D. 243 pages; 21 × 14 cm. 1953. The Year Book Publishers, Inc., Chicago. Price, $5.00.

The Digestive Tract in Roentgenology. 2nd Ed. Vol. I: Introduction; The Hypopharynx and the Esophagus; The Stomach; The Duodenum. Vol. II: The Small Intestine; The Large Intestine; Herniation and Eventration of the Diaphragm; The Gallbladder and the Bile Ducts; Spleen, Liver and Pancreas. By JACOB BUCKSTEIN, M.D., Assistant Professor of Clinical Medicine, Cornell University Medical College, etc. 1202 pages (total of both volumes); 26 × 18 cm. 1953. J. B. Lippincott Company, Philadelphia. Price, $30.00.

Grenzen des Normalen und Anfänge des Pathologischen in Röntgenbilde des Skelettes. By PROF. DR. A. KOHLER; 9th Ed. edited by DOZENT DR. E. A. ZIMMER. 672 pages; 26.5 × 18 cm. 1953. Georg Thieme Verlag, Stuttgart; agents for U. S. A.: Grune & Stratton, Inc., New York. Price, Ganzleinen DM 88.–

Influenza: A Review of Current Research. Contributors: C. H. ANDREWES—SIR MACFARLANE BURNET—Z. DEUTSCHMAN—THOMAS FRANCIS, JR.—ROSS L. GAULD—M. R. HILLEMAN—PIERRE LÉPINE—PREBEN VON MAGNUS—J. MULDER —A. M.-M. PAYNE—C. H. STUART-HARRIS—JACQUELINE H. WERNER. 223 pages; 24 × 16 cm. (paper-bound). 1954. World Health Organization, Geneva; available in U. S. A. from Columbia University Press, International Documents Service, New York. Price, $2.50.

Lehrbuch der Klinischen Hämatologie. By PROF. DR. HANS SCHUTEN. 507 pages; 24.5 × 17.5 cm. 1953. Georg Thieme Verlag, Stuttgart; agents for U. S. A.: Grune & Stratton, Inc., New York. Price, Ganzleinen DM 54.–

Medical Schools in the United States at Mid-Century. By JOHN E. DEITRICK, M.D., and ROBERT C. BERSON, M.D. 380 pages; 23.5 × 15.5 cm. 1953. McGraw-Hill Book Company, Inc., New York. Price, $4.50.

Mother and Baby Care in Pictures. 4th Ed. By LOUISE ZABRISKIE, R.N., Director, Maternity Consultation Service, New York City, etc. 244 pages; 23.5 × 15.5 cm. 1953. J. B. Lippincott Company, Philadelphia. Price, $3.00.

Official History of the Canadian Medical Services, 1939–1945. Volume Two: Clinical Subjects. Edited by W. R. FEASBY, B.A., M.D., Lieutenant-Colonel, R.C.A.M.C., Supplementary Reserve, etc.; illustrated with paintings and photographs by Canadian War Artists and Photographers. 537 pages; 26 × 17 cm. 1953. Edmond Cloutier, C.M.G., O.A., D.S.P., Ottawa, 1953, Queen's Printer and Controller of Stationery; published by authority of the Minister of National Defence, Ottawa. Price, $5.00.

Physiological Methods in Clinical Practice. The Beaumont Lecture, Wayne County Medical Society, February 2, 1953. Publication Number 216, American Lecture Series. By WILLIAM S. MIDDLETON, M.D., Department of Medicine, University of Wisconsin Medical School, Madison, Wisconsin. 40 pages; 21.5 × 14 cm. (paper-bound). 1953. Charles C. Thomas, Publisher, Springfield, Illinois. Price, $1.00.

"The Pre-Adolescent Exceptional Child": Proceedings of the 35th Conference of the Child Research Clinic of The Woods Schools, held in the Rose Garden Room of the Bellevue-Stratford Hotel, Philadelphia, Saturday, May 23, 1953. 66 pages; 23 × 15 cm. (paper-bound). 1953. Sponsored by The Woods Schools, Langhorne, Pennsylvania. Booklet available on request.

The Psychiatrist: His Training and Development. Report of the 1952 Conference on Psychiatric Education Held at Cornell University, Ithaca, New York, June 19–25, 1952. Organized and Conducted by The American Psychiatric Association and The Association of American Medical Colleges. Editorial Board: JOHN C. WHITEHORN, M.D., Chairman; FRANCIS J. BRACELAND, M.D., VERNON W. LIPPARD, M.D., and WILLIAM MALAMUD, M.D. Editorial Assistants: STELLA BLOCH HANAU and ROBERT L. ROBINSON. 214 pages; 22.5 × 14.5 cm. 1953. American Psychiatric Association, Washington, D. C. Price, $2.50.

Records and Reports of Local Health Departments: Criteria and Methods for Organization, Maintenance and Use. Public Health Monograph No. 15. By OLIVE G. JOHNSON. 89 pages; 26.5 × 20 cm. (paper-bound). 1953. U. S. Department of Health, Education, and Welfare. For sale by the Superintendent of Documents, U. S. Government Printing Office, Washington-25, D. C. Price, 45 cents.

Review of Physiological Chemistry. 4th Ed. By HAROLD A. HARPER, Ph.D., Professor of Biochemistry, University of San Francisco, etc. 328 pages; 25.5 × 17 cm. (paper-bound). 1953. Lange Medical Publications, University Medical Publishers, Los Altos, California. Price, $4.00.

Textbook of Physiology and Biochemistry. 2nd Ed. By GEORGE H. BELL, B.Sc., M.D. (Glasg.), F.R.F.P.S.G., F.R.S.E., Professor of Physiology in the University of St. Andrews at University College, Dundee; J. NORMAN DAVIDSON, M.D., D.Sc. (Edin.), F.R.F.P.S.G., F.R.I.C., F.R.S.E., Gardiner Professor of Physiological Chemistry in the University of Glasgow, etc.; and HAROLD SCARBOROUGH, M.B., Ph.D. (Edin.), F.R.C.P.E., Professor of Medicine in the Welsh National School of Medicine of the University of Wales and Director of the Medical Unit in the Royal Infirmary, Cardiff, etc.; with a foreword by ROBERT C. GARRY, M.B., D.Sc. (Glasg.), F.R.F.P.S.G., F.R.S.E., Regius Professor of Physiology in the University of Glasgow. 1002 pages; 24.5 × 17 cm. 1953. The Williams & Wilkins Company, Baltimore. Price, $10.00.

Verhandlungen der Deutschen Gesellschaft für Arbeitsschutz. Band 1. Thema: Die Fünfte Verordnung über Ausdehnung der Unfallversicherung auf Berufskrankheiten. By Dr. EDWART MAGER. 146 pages; 23 × 15.5 cm. (paper-bound). 1953. Verlag von Dr. Dietrich Steinkopff, Darmstadt. Price, Kartoniert DM 20.–

COLLEGE NEWS NOTES

Nominations for A.C.P. Elective Offices, 1954–55

In accordance with provisions of the By-Laws of the American College of Physicians, Article I, Section 3, the following nominations for the elective offices, 1954–55, are herewith announced to the Fellows and Masters of the College:

President-Elect ..... George F. Strong, Vancouver, B. C.
First Vice President ..... Marion A. Blankenhorn, Cincinnati, Ohio
Second Vice President ... George H. Lathrope, Morristown, N. J.
Third Vice President .... Ramon M. Suarez, San Juan, P. R.

Regular elections will take place at the 1954 Annual Session, Chicago, Ill., on April 8, 1954, the date of the Annual Business Meeting at the Conrad Hilton Hotel, general headquarters.

The election of nominees shall be by the Fellows and Masters. The above nominations do not preclude other nominations made from the floor at the Business Meeting.

Nominations of members of the Board of Regents and Board of Governors will be presented at the Business Meeting, as provided in the By-Laws.

Respectfully submitted,
COMMITTEE ON NOMINATIONS
Howard P. Lewis, Portland, Ore., *Chairman*
Herbert K. Detweiler, Toronto, Ont.
William C. Menninger, Topeka, Kans.
Irving S. Wright, New York, N. Y.
A. Carlton Ernstene, Cleveland, Ohio

Mead Johnson Postgraduate Scholarships

The Board of Regents of the American College of Physicians on November 14, 1953, accepted an offer of a grant of $3,000.00 from Mead Johnson & Co., of Evansville, Ind., for the foundin_ of three postgraduate scholarships in Internal Medicine, to be administered by the A.C.P. Committee on Fellowships and Awards. There shall be three awards of $1,000.00 each annually. Recipients of the awards shall be individuals who intend to practice Internal Medicine, who appear to possess the attributes for success in the practice of Internal Medicine, and who need funds to help them attain their goal of adequate education in Internal Medicine. The awards shall be open to internes or residents, with some preference, perhaps, to residents. Most individuals can arrange to get enough funds to carry them through their internships, but many may not be able to pursue an adequate residency because of lack of funds.

The Committee proposes to ask each Governor of the College to submit one nomination from his state, province or territory, to be accompanied by a letter of justification and important details.

Proposed Amendment to the By-Laws, A.C.P.

On November 15, 1953, unanimously, the Board of Regents approved the following amendment to the By-Laws, for presentation for adoption at the Annual Business Meeting of the College at Chicago on April 8, 1954:

BY-LAWS, Article XII, "Annual Convocation."

A Presidential Address will be delivered on, *or before*, this occasion.

The above Amendment will make it possible for the Presidential Address to be delivered at the Convocation or on another occasion during the Annual Session of the College.

A.C.P. Committee on Credentials

Due to illness, Dr. J. Owsley Manier, Nashville, Tenn., and Dr. George H. Lathrope, Morristown, N. J., have resigned from the Committee on Credentials and in their place Drs. A. B. Brower, Dayton, Ohio, and E. L. Amidon, Burlington, Vt., will serve until the next Annual Session.

The Committee on Credentials will meet at the College Headquarters on February 28, and at the Conrad Hilton Hotel, Chicago, on April 3, 1954. Proposals for membership should be filed in the Executive Offices of the College 60 days in advance of the meeting at which their credentials will be considered by the Committee on Credentials. Obviously, new proposals should reach the College Governor from one to four weeks in advance of the time that he must forward them to the College Office.

Coming Examinations by Certifying Boards

The American Board of Internal Medicine, William A. Werrell, M.D., Executive Secretary-Treasurer, 1 W. Main St., Madison 3, Wis.

The following oral examinations have been scheduled by the American Board of Internal Medicine for 1954:

New Orleans—Feb. 2–5, 1954,
Chicago—April 1–3, 1954,
Los Angeles—June 15–17, 1954,
New York City—Sept. 22–24, 1954.

The closing date for acceptance of applications for the examinations at New Orleans, Chicago, and Los Angeles was January 2. The closing date for acceptance of applications for the New York City examination will be April 1.

May 1 will be the closing date for the written examination of the Board, which will be held October 18, 1954.

The American Board of Pediatrics, John McK. Mitchell, M.D., Executive Secretary, 6 Cushman Rd., Rosemont, Pa.

Oral Examinations: Washington—Feb. 19–21, 1954,
Des Moines—March 19–21, 1954.

A.C.P. Regional Meetings

Regional Meetings of the College during November of 1953 were markedly successful both in regard to the quality of the programs and the large participation of members and guests.

Puerto Rico

The Puerto Rico Regional Meeting was held at San Juan, November 20–21, 1953, under the Governorship of Dr. Rafael Rodriguez-Molina. The program on November 20 was held in the Headquarters Building of the Puerto Rico Medical Association;

the program on Saturday, in the University of Puerto Rico School of Medicine Building. The scientific program was an exceedingly interesting one, presented by Associates and Fellows of the College and by a number of invited guests, among whom was Dr. E. Harold Hinman, Dean of the Medical School, who spoke on "Medical Education in Puerto Rico." On Saturday, November 21, a luncheon was given at the School of Medicine and in the evening Dr. Rodriguez-Molina gave a reception and buffet dinner at the San Juan Country Club. On the formal program President-Elect Cyrus C. Sturgis, Ann Arbor, Mich., presented a paper on "Treatment of the Anemias," and Mr. Edward R. Loveland, Executive Secretary of the College, Philadelphia, gave an address on the work of the College. Miss Pearl M. Ott, Executive Assistant, Philadelphia, was among the honored guests. There were more than 100 physicians in attendance at the meetings, although the official registration was 81.

Midwest

The Midwest Regional Meeting, embracing the States of Illinois, Indiana, Iowa, Minnesota and Wisconsin, was held at Milwaukee, November 21, 1953, under the Governorship of Dr. Karver L. Puestow, Madison, Wis., and the General Chairmanship of Dr. Francis D. Murphy, F.A.C.P., of Milwaukee. Dr. Joseph W. Rastetter, F.A.C.P., of Milwaukee, was Chairman of Arrangements, and many of the Milwaukee and nearby members of the College served on active committees. The attendance numbered 136 Fellows, 99 Associates, 193 guests; 428. The entire program was conducted at the Schroeder Hotel, and the College Governors for the various states represented presided over certain sections of the program.

The pattern of this program is a large number of 15-minute papers, presented by Associates, Fellows and specially invited guests. The General Electric X-Ray Company provided coffee at intermissions and the Blatz Brewing Company of Milwaukee —Schenley Division, provided music and entertainment at the banquet in the evening. Dr. Karver L. Puestow, F.A.C.P., Governor for Wisconsin was the Toastmaster at the Banquet, and distinguished guests included Rev. Anthony F. Berens, S. J., Regent of Marquette University School of Medicine; Dr. LeRoy H. Sloan, F.A.C.P., President of the College, Chicago; Dr. William S. Middleton, M.A.C.P., past President of the College, Madison; Dr. Walter L. Palmer, F.A.C.P., Regent of the College, Chicago; Dr. Edward C. Reifenstein, Sr., F.A.C.P., College Governor for Western New York, Syracuse; and Dr. John S. Hirschboeck, F.A.C.P., Dean of Marquette University School of Medicine, Milwaukee.

North Carolina

North Carolina held its 20th Anniversary Regional Meeting at Chapel Hill, N. C., December 3, 1953, under the Governorship of Dr. Elbert L. Persons, F.A.C.P., Durham. Dr. Edward McG. Hedgpeth, F.A.C.P., was Chairman of the Committee on Arrangements and Dr. Charles W. Styron, F.A.C.P., Raleigh, was Chairman of the Program Committee. The program was conducted at the North Carolina Memorial Hospital, an integral unit of the University of North Carolina School of Medicine. In view of the fact that this was the 20th Anniversary of the beginning of Regional Meetings in the College as well as in North Carolina, a program of particular excellence was arranged. Dr. Wallace M. Yater, F.A.C.P., Regent of the College, Washington, D. C., addressed the Banquet at the Carolina Inn on the objectives and activities of the College, and Mr. Edward R. Loveland, Executive Secretary, Philadelphia, addressed the banquet on the history of the College during the last 20 years, with particular emphasis on the part North Carolina has played. A very large proportion of the Fellows and Associates in North Carolina were in attendance and there were many guests, the total being approximately 200. Inasmuch as Mr. Loveland had

attended the first Regional Meeting in North Carolina in 1933 and was again present at its Twentieth Anniversary, Dr. Paul Whitaker on behalf of the North Carolina members presented a Parker Pen desk set with an engraved gold plate on the base, "North Carolina Region, A.C.P., 1933–1953—Edward R. Loveland."

Michigan

The State of Michigan for several years was an integral part of the Midwest Regional Meeting area. In early 1953 the Michigan members voted to conduct their own individual Regional Meeting, Dr. H. Marvin Pollard, Governor for Michigan, was appointed General Chairman, Dr. William W. Reveno, F.A.C.P., Detroit, was appointed Chairman of the Program Committee, and Ann Arbor was selected as the site of the meeting. An all-day program was conducted in H. H. Rackham Building of the University of Michigan on Saturday, December 5, 1953, with members from all parts of the state represented on the program, along with a number of guests who had interesting subjects to present. Dr. Pollard presided at the opening session followed by Dr. Douglas Donald, F.A.C.P., former Governor for Michigan, at the second session, Dr. William M. LeFevre, F.A.C.P., Muskegon, at the Third Session, and Dr. Cyrus C. Sturgis, F.A.C.P., President-Elect of the College, Ann Arbor, at the fourth session. A reception and banquet was held in the evening at the Allenel Hotel, with Dr. Pollard, as Governor, presiding. Guest speakers at the banquet included Dr. LeRoy H. Sloan, President of the College, Chicago; Dr. Cyrus C. Sturgis, President-Elect of the College, Ann Arbor, and Mr. Edward R. Loveland, Executive Secretary of the College, Philadelphia. Among other honored guests were Dr. Donald, Dr. Karver L. Puestow, College Governor for Wisconsin, Madison, and Dr. Howard Wakefield, College Governor for Northern Illinois, Chicago. Some 200 physicians were in attendance and all were thoroughly favorable to a continuation of the individual Regional Meeting for Michigan in the future. Yet to be determined is the meeting place for these Regional Meetings in Michigan—whether they shall be held at a somewhat central location, such as Ann Arbor, or shall alternate among three of the larger centers, such Grand Rapids, Ann Arbor and Detroit.

A.C.P. Regional Meetings, 1954

Eastern Pennsylvania—Philadelphia, January 15
Maryland-District of Columbia—Baltimore, January 16
Colorado—Colorado Springs, January 22–23
Southern California, Riverside—February 13–14
Virginia—Richmond, February 25
Nebraska—Lincoln, February 27
Kansas—Topeka, March 19
Southern Illinois—Peoria, March ?
Northern California—San Francisco, June 16
North Dakota—Bismarck, September 11
New England—Hartford, Conn., October 22
New Jersey—Newark, November 3

Numerous other Regional Meetings are in process of being planned and will be announced as the dates are determined.

The American Cancer Society, 47 Beaver St., New York 4, N. Y., has announced the VIth International Cancer Congress at Sao Paulo, Brazil, July 23–29, 1954. Full details concerning the program and travel accommodations may be obtained from the above office.

A.P.A. Establishes Committee on Certification

Under the Presidency of Dr. Kenneth E. Appel, F.A.C.P., Philadelphia, The American Psychiatric Association has recently established a committee to certify physicians as "qualified mental hospital administrators." The Committee will conduct examinations periodically and issue qualification certificates to successful applicants.

According to Dr. Appel, the step has been taken to help ensure that the chief executives of mental hospitals shall not only be physicians adequately trained in psychiatry, but that they shall also be skilled in business and personnel management, community relations, budget control, procurement, and other essential administrative techniques.

Dr. Francis J. Braceland, F.A.C.P., Hartford, Conn., is Chairman of this new Committee on Certification of Mental Hospital Administrators. Other members include Dr. William B. Terhune, F.A.C.P., New Canaan, Conn., Dr. Walter H. Baer, F.A.C.P., Peoria, Ill., and Dr. Granville L. Jones, F.A.C.P., Williamsburg, Va. Dr. C. N. Baganz, F.A.C.P., Manager of the Veterans Administration Hospital, Lyons, N. J., is Secretary of the Committee, and application forms for certification and other information may be obtained from him.

American College of Radiology Honors Dr. Benjamin Orndoff

Dr. Benjamin H. Orndoff, F.A.C.P., Chicago, was the recipient of one of two gold medals awarded by the American College of Radiology at the annual banquet in Chicago on Feb. 5, 1954. Dr. Orndoff received the award "for distinguished and extraordinary service to the American College of Radiology and to the profession for which it stands." A past President of the American College of Radiology and the Radiological Society of North America, Dr. Orndoff is Professor of Radiology and Head of the Department at Loyola University School of Medicine. He has been a Fellow of the American College of Physicians since 1920.

Dr. David T. Smith, F.A.C.P., Professor of Bacteriology and an Associate Professor of Medicine, Duke University School of Medicine, Durham, N. C., has been elected a member of the Sub-Specialty Board in Pulmonary Diseases of the American Board of Internal Medicine for a term of five years, to July 1, 1958, succeeding Dr. Donald S. King, F.A.C.P., of Brookline, Mass.

Dr. Ludwik Gross (Associate), New York City, received the Robert Roesler de Villiers award for his contributions to the knowledge of the nature and cause of leukemia. The award was presented Oct. 20, 1953, in ceremonies held in the New York Academy of Medicine. Dr. Maxwell M. Wintrobe, F.A.C.P., Salt Lake City, and Dr. William B. Castle, F.A.C.P., Boston, spoke about leukemia research. Dr. Gross was formerly associated with the Pasteur Institute in Paris for seven years and is now Chief of Research at the Veterans Administration Hospital, Bronx, N. Y. Dr. Gross' paper was among 226 submitted from 22 countries in 6 languages.

Dr. Frank H. Krusen, F.A.C.P., Rochester, Minn., will receive the Second Annual Physician's Award from the President's Committee on Employment of the Physically Handicapped during the annual meeting of the Congress on Industrial Health at Louisville, Ky., Feb. 23–24, 1954. Dr. Krusen, who is Head of the Section on Physi-

cal Medicine at the Mayo Clinic and who has been Professor of Medicine at the Mayo Foundation since 1935, recently received his state's award of merit for his contributions to employment through rehabilitation of physically handicapped persons.

Dr. James S. McLester, Sr., F.A.C.P., Birmingham, Ala., received the Joseph Goldberger award for outstanding contributions in the field of clinical nutrition during the recent meeting of the American Medical Association in St. Louis. A former President of the A.M.A. and an ex-Regent of the College, Dr. McLester was honored "for the outstanding rôle he has played in translating the results of nutrition research into human values and in the integration of nutrition into the teaching of all phases of medicine." The award was presented by the A.M.A. through its Council on Foods and Nutrition, and includes a gold medal and $1,000.00.

Dr. J. Warrick Thomas, F.A.C.P., Richmond, Va., has been chosen Vice President of the recently organized American Foundation for Allergic Diseases. Dr. Oscar Swineford, Jr., F.A.C.P., Charlottesville, is among the Trustees. The Foundation is sponsored by the American Academy of Allergy and the American College of Allergists.

Dr. Howard Wakefield, F.A.C.P., Chicago, was recently elected Chairman of the Department of Medicine of St. Luke's Hospital.

Dr. Norbert J. Roberts (Associate), Philadelphia, Medical Director of the Pennsylvania Railroad, has been appointed Assistant Professor of Occupational Medicine at the University of Pennsylvania School of Medicine.

At the recent annual meeting of the West Virginia Heart Association in Charleston, Dr. Walter C. Swann, F.A.C.P., Huntington, was installed as President. Dr. Richard N. O'Dell (Associate), Charleston, and Dr. William E. Bray, Jr., (Associate), Huntington, were elected Vice President and Secretary, respectively.

At the annual dinner and business meeting of the Omaha Mid-West Clinical Society on Dec. 14, 1953, Dr. Friedrich W. Niehaus, F.A.C.P., was chosen President-Elect. Dr. Joseph D. McCarthy, F.A.C.P., College Governor for Nebraska, was re-elected Counselor.

The 1954 annual clinical assembly will be held Oct. 25–28, and in 1955 the assembly will be held Oct. 24–27.

Dr. L. Emmet Madden, F.A.C.P., Columbia, S. C., has recently been appointed a a member of the State Board of Medical Examiners.

Dr. Thomas S. Edwards (Associate), Charlottesville, and Dr. William A. Read, F.A.C.P., Newport News, are Vice Presidents of the Virginia Diabetic Association.

Dr. Herbert Pollack, F.A.C.P., New York City, has recently been elected President of the New York Diabetes Association.

Dr. Delivan A. MacGregor, F.A.C.P., Wheeling, has been appointed Chairman of the West Virginia Board of Health for a two-year term.

Dr. George F. Evans, F.A.C.P., Clarksburg, was recently elected Vice President of the West Virginia Trudeau Society.

Dr. George F. Schmitt, F.A.C.P., Miami, Fla., is a Registered Parliamentarian, being the only physician of whom we know who has qualified by taking the prescribed examination.

Dr. William Rottersman (Associate), Topeka, Kans., was recently elected a Councilor of the Mid-Continent Psychiatric Association at its annual meeting in Kansas City, Mo.

Dr. Ejvind P. Fenger, F.A.C.P., Minneapolis, was recently named President-Elect of the Mississippi Valley Trudeau Society, and Dr. Leon J. Galinsky, F.A.C.P., Des Moines, Iowa, was elected Vice President.

Dr. Louis N. Katz, F.A.C.P., Chicago, was chosen Vice President of the American Society for the Study of Arteriosclerosis at the recent annual meeting in Chicago.

Dr. Wallace M. Yater, F.A.C.P., Washington, D. C., a Regent of the College, was recently appointed to the National Advisory Health Council for the National Microbiological Institute. The Council acts in an advisory capacity to Dr. Leonard A. Scheele, F.A.C.P., Surgeon General of the U. S. Public Health Service, on grants made by the Institute.

Dr. Lewis B. Flinn, F.A.C.P., Wilmington, Del., was chosen President-Elect of the Medical Society of Delaware at the recent annual meeting in Wilmington.

Dr. Arnold F. Strauss (Associate), Norfolk, Va., was made a corresponding member of the Peruvian Society for Pathology during his recent visit to Peru.

Dr. Arthur M. Freeman, F.A.C.P., Birmingham, was promoted from Assistant Professor of Medicine to Associate Professor of Medicine at the Medical College of Alabama last October.

Dr. Nathan Blumberg, F.A.C.P., has resigned as Associate Professor of Medicine at Temple University School of Medicine, Philadelphia, and has been appointed Professor of Clinical Medicine (Geriatrics) at the Hahnemann Medical College and Hospital of Philadelphia.

Dr. Charles M. Gruber, F.A.C.P., formerly of Philadelphia, has recently been appointed Head of the Department of Pharmacology at the College of Medical Evangelists, Loma Linda, Calif. A past President of the American Society for Experimental Biology and Medicine, Dr. Gruber had been Professor of Pharmacology at Jefferson Medical College of Philadelphia since 1932.

Dr. Martin S. Buehler, F.A.C.P., Dallas, Tex., retired in December, 1953, as National Surgeon of the Reserve Officers Association of the United States. Dr. Buehler was elected President of the Texas Academy of Internal Medicine at its recent annual meeting.

Dr. Robert H. Bayley, F.A.C.P., Oklahoma City, Professor of Medicine at the University of Oklahoma School of Medicine, Dr. Arthur Grollman, F.A.C.P., Dallas,

Professor of Experimental Medicine at the Southwestern Medical School of the University of Texas, and Dr. George R. Herrmann, III, F.A.C.P., Galveston, Professor of Medicine at the University of Texas School of Medicine, were among the visiting lecturers in a course on recent advances and current problems in cardiology. The course was sponsored by Baylor University College of Medicine and the University of Texas Postgraduate School of Medicine during Heart Week, Feb. 15–19, 1954.

Dr. Henry Bockus, F.A.C.P., Philadelphia (Gastro-enterology), Dr. A. Carlton Ernstene, F.A.C.P., Cleveland (Cardiology), Dr. Alexander Marble, F.A.C.P., Boston (Diabetes), Dr. E. J. Stieglitz, F.A.C.P., Washington, D. C. (Geriatrics), and Dr. T. E. Woodward, F.A.C.P., Baltimore, were among the guest speakers at the Mid-South Postgraduate Medical Assembly held Feb. 9–12, 1954, at Memphis, Tenn.

Dr. Rudolph H. Kampmeier, F.A.C.P., Nashville, Tenn., discussed "The Variability of Diffuse Arteritis (Collagen Diseases)" at the annual assembly of the Puerto Rico Medical Association, which met in Santurce Dec. 9–13, 1953.

Col. Carl W. Tempel, (MC), USA, F.A.C.P., Denver, and Dr. Oscar Auerbach, F.A.C.P., East Orange, N. J., were among the participants in a symposium on tuberculosis, which was part of the program at the annual meeting of the Baltimore City Medical Society, held Dec. 18, 1953. Col. Tempel is Chief of Medical Service at Fitzsimons Army Hospital and Dr. Auerbach is Chief of Laboratory Service at the Veterans Administration Hospital, East Orange.

Dr. E. Kost Shelton, F.A.C.P., Clinical Professor of Medicine at the University of California at Los Angeles, addressed the Honolulu (Hawaii) County Medical Association on the subject, "Modern Concepts of Clinical Endocrinology," on the evening of February 6, 1954.

Dr. William B. Bean, F.A.C.P., Iowa City, Dr. Edward G. Billings, F.A.C.P., Denver, Dr. Thomas J. Dry, F.A.C.P., Rochester, Minn., and Dr. Douglas H. Sprunt, Sr., F.A.C.P., Memphis, will be among the honored guests at the Spring Clinical Conference of the Dallas Southern Clinical Society, to be held March 15–18, 1954.

Dr. Alexander B. Gutman, F.A.C.P., New York City, spoke on "Gout" in the auditorium of the Kansas City (Mo.) Municipal Hospital Number One on December 17, 1953.

Dr. Paul D. White, F.A.C.P., Boston, delivered the First Annual Harry G. Remer Lecture on rheumatic fever at La Rabida Sanitarium, Chicago, December 11, 1953.

Dr. Herman Beerman, F.A.C.P., Philadelphia, Chief of the Dermatology Service at the Graduate Hospital of the University of Pennsylvania and Head of the Department of Dermatology at the Pennsylvania Hospital, lectured at the meetings of the American Academy of Dermatology and Syphilology in Chicago in December and later addressed a meeting of the Bronx (N. Y.) Dermatological Society.

Dr. Julius H. Comroe, Jr., F.A.C.P., Philadelphia, recently participated in a panel on chronic pulmonary disease at the New York Academy of Medicine.

Dr. Wright R. Adams, F.A.C.P., Chicago, spoke on "Pulmonary Hypertension" at the December 15 joint meeting of the Allegheny County Medical Society (Pittsburgh) and the Western Pennsylvania Heart Association.

Dr. Meyer Naide, F.A.C.P., Philadelphia, was among the out-of-state speakers at the annual meeting of the Delaware Academy of General Practice, held Dec. 12, 1953, in Wilmington. His subject was "Drugs and Procedures in Treatment of Peripheral Vascular Diseases." Dr. Thomas M. Durant, F.A.C.P., Philadelphia, discussed "Pathophysiology and Treatment of Congestive Heart Failure," and Dr. James L. A. Roth (Associate), Philadelphia, spoke on "Useful Medications in Gastroenterology."

"Roentgenology of the Normal and the Abnormal Heart" was the subject used by Dr. John B. Schwedel, F.A.C.P., Assistant Clinical Professor of Medicine at Columbia University College of Physicians and Surgeons, when he addressed the Illinois Chapter of the American College of Chest Physicians in Chicago, Dec. 11, 1953.

Dr. Louis F. Bishop, F.A.C.P., New York City, recently addressed the members of the New London (Conn.) Heart Association on "Common Complications of Myocardial Infarction."

Under the Presidency of Dr. Amadeo Vicente-Mastellari, F.A.C.P., Panama, R. P., the Fourth Central American Congress of Tuberculosis was held in Panama, Nov. 30–Dec. 4, 1953. Representatives of Central American Countries, Santo Domingo, and Haiti were present as well as delegates from the National Tuberculosis Association, the Inter-American Coöperative Service of Public Health, and the World Health Organization. Subjects discussed included progress of tuberculosis campaigns, BCG vaccines, and thoracic surgery. Dr. Vicente-Mastellari has recently been appointed Professor of Phthisiology at the School of Medicine of the National University.

Dr. Samuel Cohen, F.A.C.P., was appointed Director of Medicine at the B. S. Pollak Hospital for Chest Diseases, Jersey City, New Jersey, on December 14, 1953.

Dr. Samuel Baer, F.A.C.P., of Philadelphia, was recently elected Senior Attending Physician in the Department of Medicine of the Albert Einstein Medical Center, Philadelphia, and Cardiologist of the Northeastern Hospital, Philadelphia.

OBITUARIES

DR. ALEXANDER G. BROWN, JR.

Dr. Alexander Gustavus Brown, Jr., F.A.C.P., Richmond, Va., who died Sept. 16, 1953, after a brief illness, was born in Ashland, Va., in 1873.

After attending Randolph-Macon College, where his father was Secretary for many years, he studied medicine at the University College of Medicine, where he graduated in 1898.

At his death Dr. Brown was Emeritus Associate Professor of Medicine, Medical College of Virginia, and a prominent internist on the staff of Stuart Circle Hospital. He was always most active in medical affairs in his city and state, having been editor of the *Virginia Medical Monthly* for fourteen years as well as a past President of the Richmond Academy of Medicine and a Diplomate of the American Board of Internal Medicine.

He was elected a Fellow of the American College of Physicians in 1920 and as such was a member of the College almost as long as any other individual in Virginia.

Dr. Brown remained active in practice until a short time before his death and was greatly beloved by both the members of his profession and his hosts of patients and friends by whom he will be long remembered.

CHARLES M. CARAVATI, M.D., F.A.C.P.,
Governor for Virginia

REAR ADMIRAL ARTHUR WHITE DUNBAR, (MC), USN (RETIRED)

Rear Admiral Arthur White Dunbar, Medical Corps, USN, retired inactive, F.A.C.P., died at the Naval Hospital, Philadelphia, Pa., on Nov. 6, 1953. His age was 84.

Born in Cannon Falls, Minn., on Sept. 7, 1869, Admiral Dunbar received his degree of Doctor of Medicine from the University of California Medical School in 1891.

Commissioned an Assistant Surgeon in the Medical Corps of the Navy on Oct. 10, 1894, he was promoted to Passed Assistant Surgeon on Oct. 10, 1897; to Surgeon, March 3, 1903; to Medical Inspector with the rank of Commander, Aug. 29, 1916; to Medical Director with the rank of Captain, Jan. 1, 1918; and to Rear Admiral, Medical Corps, on April 18, 1932, to rank from Dec. 7, 1926.

Admiral Dunbar, while serving on the *USS San Francisco*, participated in the blockade of Havana, Cuba, in the Spanish-American War. As commanding officer of the *USS Relief*, he made the world cruise with the Great White Fleet. During World War I, he commanded the hospital ships *USS Comfort* and *USS Repose*. He also served, during his nearly 39 years of naval service, on the United States Ships *Resolute, Newark, Monongahela, Wyoming, California, Tennessee,* and *Missouri*—serving as Fleet Surgeon on the *USS Tennessee*. He commanded the Naval Hospitals at Philadelphia and Annapolis, twice served as Inspector of East Coast Naval Medical Department Activities, and was Assistant Chief of the Navy's Bureau of Medicine and Surgery from April, 1925, to June, 1927.

Admiral Dunbar, who became a Fellow of the American College of Physicians in 1923, was placed on the retired list of officers of the Navy on Oct. 1, 1933.

Services were held in the Fort Myer Chapel on Tuesday, Nov. 10, 1953, followed by burial with full military honors in Arlington National Cemetery.

Technical Information Office,
Bureau of Medicine and Surgery,
Navy Department.

DR. EDWIN W. GEHRING

Edwin Wagner Gehring, C.E., M.D., Fellow of The American College of Physicians since 1917 and first governor of the College from Maine, died at his home in Portland on August 8, 1953.

He was born at Cleveland, Ohio, March 3, 1876. His early years were spent there, but he came to Maine for his health and attended Gould Academy in Bethel. He studied three years at the Massachusetts Institute of Technology, then transferred to Cornell University, where he was graduated a civil engineer in 1900. He turned then from the field of engineering and studied medicine, first at Harvard Medical School and then at Bowdoin Medical School, where he graduated in 1904.

He served as intern for one year at the Maine General Hospital. Later there were periods of study in London, Vienna, and Berlin. He taught Physiology and Internal Medicine at Bowdoin Medical School.

For many years Dr. Gehring was a member of the staff of the Maine General Hospital. He was Chief of Medical Service from 1928 to 1937. For years he served as consultant to many of the smaller hospitals in southern and western Maine. He was at various times President of the Portland Medical Club, President of the Cumberland County Medical Society, Councilor of the Maine Medical Association, and in 1934–35 President of the Maine Medical Association. In 1935–36 he served as Editor-in-Chief of the *Maine Medical Journal*.

Dr. Gehring was a man of many talents. He was a busy and able consultant in Internal Medicine. He accepted the responsibilities of office in the organized medical societies. He was a staunch member of the State Street Congregational Church and served there as Deacon. He had a wide acquaintance with the best in literature and in music. On many occasions he used his ability in public speaking for the delight of medical and lay groups alike. The American College of Physicians and the state of Maine recognize the loss of an outstanding medical citizen.

RICHARD S. HAWKES, M.D., F.A.C.P,
Governor for Maine

DR. CLARENCE AUSTIN SMITH

Clarence Austin Smith, M.D., F.A.C.P., died at his home in Seattle, Wash., Sept. 10, 1953, two days after suffering a cerebral hemorrhage.

Dr. Smith was born in Derby, Conn., Jan. 24, 1861, and received his Bachelor of Arts Degree from Yale University in 1882. For the next two years he taught at the Cayuga Lake Military Academy, Aurora, N. Y., before matriculating at Columbia University College of Physicians and Surgeons, where he received his M.D. Degree in 1887. Following his internship and residency at Bellevue Hospital, Dr. Smith moved to Seattle in 1889, where he performed the duties of a general practitioner with Dr. James B. Eagleson. In addition, from 1886 to 1899 he was a member of the Washington State Examining Board and served as Health Officer for the City of Seattle from 1897 to 1899. He was also President of the King County Medical Society in 1898.

In 1899, Dr. Smith went to Johns Hopkins University School of Medicine and during the period 1901–02 was Assistant in Pathology and Bacteriology at Georgetown Medical College.

Dr. Smith returned to Seattle in 1902 and was one of the men responsible for founding the Washington Library Association in that year. Intent upon the dissemination of medical knowledge, Dr. Smith was largely responsible for *Northwest Medicine*, which was first published in 1902 and which he edited for almost 50 years.

In 1909 the Washington State Medical Association elected him President; and for 4 years at the time of the First World War, he served as Contract Surgeon for the U. S. Army.

In 1924 he became interested in physical medicine and from then until his retirement from active practice in 1937, he specialized in this field.

Dr. Smith was a member of the American College of Physical Therapy and the American Medical Association. He became a Fellow of the American College of Physicians in 1922.

Furnished through the courtesy of *Northwest Medicine* and GEORGE H. ANDERSON, M.D., F.A.C.P., Governor for Washington

DR. H. MASON SMITH

H. Mason Smith, M.D., F.A.C.P., died suddenly on June 16, 1953, in Tampa, Florida, while apparently convalescing from a massive intestinal hemorrhage. He had retired from active practice a year previously on account of cardiac disability.

Dr. Smith was born at Douglasville, Georgia, May 10, 1884. He graduated from the University of Georgia Medical Department in 1908. Postgraduate work was done at the New York Post-Graduate Medical School and Hospital, New York Neurological Institute and Harvard Medical School. He was certified by the American Board of Psychiatry and Neurology.

He was superintendent of the Florida State Hospital from 1914 to 1917 and served as a First Lieutenant in the Medical Corps of the U. S. Army in 1917–18 after which he entered private practice of neuropsychiatry in Tampa, Florida, where he lived until his death.

He was consulting neuropsychiatrist for the Atlantic Coast Line Railroad and chief of the neuropsychiatric service of the Tampa Municipal Hospital from 1921 to 1947 where his influence through these many years anticipated the "modern" concepts of integrated comprehensive psychiatric service in a general hospital.

Dr. Smith was a greatly beloved and influential member of the Florida State Medical Association and served as its president in 1926–27 at which time it was a rare and signal honor for a psychiatrist to be so recognized by the medical profession at large.

His contributions to medical literature included early (1937) articles in several journals on the "hypoglycemic" therapy of schizophrenia and papers on sleep disturbances and Menière's disease.

In 1947 he founded the Mason Smith Neurological Clinic of Tampa which organization proudly retains his name and continues his precepts of closely integrating psychiatry with the medical practice of the community.

He is survived by his wife and one son who live in Tampa.

WILLIAM C. BLAKE, M.D., F.A.C.P.,
Governor for Florida

DR. HORACE W. SOPER

Horace Wendell Soper, M.D., F.A.C.P., was born in Hillsboro, Ill., in 1867. This was fourteen years after the death of William Beaumont and 28 years before Roentgen discovered the short wave ray. Beaumont took advantage of a unique opportunity to investigate some of the processes of digestion. Roentgen's discovery gave to men of science a new tool which enabled them to filch from nature some of her best guarded secrets. These achievements are two of the fundamental building stones on which gastro-enterology is built. In this field Horace Soper was most interested and active during his career as a physician.

After graduation from the Washington University School of Medicine in 1894, he engaged in general practice for ten years. He then decided to devote himself

to the young specialty of gastro-enterology. He took stock, and realizing the deficiencies in his training, especially in gross and microscopic pathology, and desiring study under the then leaders in diseases of the digestive tract, he went to Europe and spent two years in Berlin and Vienna.

He returned to St. Louis in 1908. The background of ten years in general practice and then two years of intensive study in special fields equipped him to devote himself to the practice of gastro-enterology. In 1908, a new inspiration became a factor in his Weltanschauung. He married Mary Reynolds Halcombe. For 45 years, she was in the truest sense of the word his helpmate, an ever quickening stimulus to a well-rounded life.

He had one of the first, probably the first, x-ray machine in St. Louis. This, when compared to modern equipment, was like the Model T compared with our present-day automobile. The fluoroscopic screen enabled only one person at a time to make observations. Dr. Soper and his associate, Walter Mills, made the most of the tools available and established a clinic for diagnosis and treatment, laying most stress on the diseases of the digestive tract.

Dr. Soper was a kindly, courteous, considerate gentleman. His patients had confidence in him, inspired by his professional skill and personal interest. Dignified in his bearing, he had a kindly wit, and the glint in his eye frequently bespoke his awareness of the incongruities of life. He defended a thesis, especially a controversial one, with vigor, but never with asperity.

During his long years of practice, he held many positions as teacher and member of hospital staffs. Among them were the following: Demonstrator in Anatomy, Washington University School of Medicine; Chief of Medical Clinic, St. John's Hospital; member of staff, St. Luke's Hospital, DePaul Hospital and Jewish Hospital. He was Secretary and later Chairman of the Section on Proctology and Gastro-enterology of the American Medical Association. He was a Diplomate of the American Board of Internal Medicine. He was a member of the American Medical Association, Mississippi Valley Medical Society, American Gastro-Enterological Association and the National Society for the Advancement of Gastro-Enterology. He was a Fellow of the American College of Physicians from 1924.

Horace Soper died Sept. 27, 1953, in his 86th year, after an illness lasting four days. Age did not wither his interest in people, in English literature or in medicine.

LLEWELLYN SALE, SR., M.D., F.A.C.P.

DR. EDSON H. STEELE

Edson Hun Steele, M.D., F.A.C.P., was born in Monguap Valley, N. Y., March 5, 1895, and died in Los Angeles on June 25, 1953, after a few hours' illness while he was at work at the hospital. He attended Union College in Schenectady, N. Y., and graduated from Albany Medical College in 1919.

Dr. Steele came to Los Angeles in 1922. He was Associate Clinical Professor of Nervous Diseases (Psychiatry) at the College of Medical Evangelists; Consulting Psychiatrist, Los Angeles County Hospital and Resthaven Sanitarium, as well as Attending Psychiatrist at the Charter Oak Lodge in Covina, Calif.

He was Past President of the Los Angeles Society of Neurology and Psychiatry. He entered on active duty with the Medical Corps, U.S.N.R., in January, 1942, and was with combat troops at Guadalcanal and the Solomon Islands. At the time of discharge from the Navy in October, 1945, he was Chief Psychiatrist, U. S. Naval Hospital, Treasure Island, Calif.

He had been in private practice since July, 1946. He was a Diplomate of the American Board of Psychiatry and Neurology and became a Fellow of the American College of Physicians in 1947.

Dr. Steele is survived by his widow, Mrs. Aileen Steele; his mother, Mrs. Gertrude Steele and three sisters, Mmes. Gertrude Fredericks, Wilamina Lange and Janet Randall.

LELAND HAWKINS, M.D., F.A.C.P.,
Governor for Southern California

DR. C. W. STRICKLER, SR.

Dr. Cyrus Warren Strickler, Sr., F.A.C.P., died of renal insufficiency on July 23, 1953, in Atlanta, Ga.

He was held in highest esteem by his colleagues, his many patients, and civic-minded citizens. He was able to continue actively in his inspiring medical career until three months before his death.

He was born on Nov. 1, 1873, in Augusta County, near Staunton, Va., and moved to Atlanta in his youth with his parents, Dr. and Mrs. G. B. Strickler. In 1903 he married Miss Anne Virginia Williams and is survived by his wife and two sons, Givens Brown Strickler and Dr. Cyrus Warren Strickler, Jr., F.A.C.P.

Dr. Strickler attended Washington and Lee University, the Atlanta College of Physicians and Surgeons (now Emory University School of Medicine), from which he graduated with first honors in 1897. His postgraduate medical training was received at the Elkin Cooper Sanitarium and the Grady Memorial Hospital in Atlanta, where he began his practice in 1901, limiting it to internal medicine in 1908.

From the earliest years of his practice, Dr. Strickler participated enthusiastically on the teaching staff of the medical school. He is fondly remembered by hundreds of medical students as one of the most capable and inspiring teachers of internal medicine. He was Professor of Clinical Medicine at Emory University School of Medicine until shortly before his death.

In the First World War he served with the Emory Unit, which was designated as Base Hospital 43. He was Chief of the Medical Service with rank of Major, and later, as Lieutenant Colonel, became the unit's executive officer. For his outstanding service with the armed forces, he was awarded the honor of Officier d'Académie. This honor was conferred by the Ministère de l'Instruction Publique et des Beaux-Arts.

Dr. Strickler was a member and past President of the Fulton County Medical Society, a member of the Medical Association of Georgia, the Southern Medical Association, the American Medical Association, the Association for the Study of Internal Secretions and the Fifth District Medical Society, a Diplomate of the American Board of Internal Medicine and a Fellow of the American College of Physicians since 1920.

He contributed numerous scientific publications dealing with many subjects in internal medicine.

Dr. Strickler's passing ends a long and useful career in the practice and teaching of internal medicine, and he will be sorely missed by his many admirers.

CARTER SMITH, M.D., F.A.C.P.,
Governor for Georgia

DR. DAVID TURNOFF

Dr. David Turnoff, Associate of the College, Philadelphia, Pa., died on June 14, 1953, of a heart attack while driving his automobile. He was born in Philadelphia, March 14, 1912; held an A.B. degree and an M.D. degree from the University of Pennsylvania. He interned at the Philadelphia General Hospital, and later was a member of its staff. He served in World War II for four years, retiring with the rank of Major. He was Assistant Visiting Physician at the Philadelphia General

Hospital, Chief of Medical Service at the Nazareth Hospital, Chief of Medicine at the Kensington Hospital and at one time was associated with the Philadelphia Institute for Medical Research. Dr. Turnoff was a member of the Philadelphia County Medical Society, the Pennsylvania State Medical Society, American Heart Association and the American Medical Association. He had been an Associate of the American College of Physicians since 1949, and was in the process of qualifying for Fellowship.

DR. JOHN F. WHALEN

Dr. John Francis Whalen, F.A.C.P., was born in New Brunswick, N. J., on November 18, 1900, and died in his home in Altadena, Calif., on July 3, 1953, of a coronary thrombosis.

He attended Catholic University of America and then entered Jefferson Medical College of Philadelphia, receiving his M.D. degree in 1927. Dr. Whalen came to California following his graduation and received his intern and resident training in the Los Angeles County Hospital. He continued at this institution as Attending Physician and was an Instructor in Medicine at the University of Southern California School of Medicine until 1936. He had been a member of the staff of St. Luke Hospital in Pasadena since 1933, where he was Chairman of the Board of Directors and President of the Staff.

Dr. Whalen had served as Secretary, President and Chairman of the Executive Board of the Pasadena Medical Society and was a Past President of the Pasadena branch of the Los Angeles County Medical Society. He became a Fellow in the American College of Physicians in 1944 and was also a Diplomate of the American Board of Internal Medicine.

Dr. Whalen is survived by his widow, Mrs. Mary B. Whalen, and five children, Jane, John, Ann, Elizabeth and Lawrence.

It is with sincere regret that we record his passing.

LELAND HAWKINS, M.D., F.A.C.P.,
Governor for Southern California

DR. ARTHUR T. WYATT

Arthur T. Wyatt, M.D., a Fellow of the College since 1939, because of illness retired in 1949 to his birthplace, Raleigh, N. C., and died there of coronary occlusion, Oct. 3, 1953.

After premedical education at the University of North Carolina, he received his M.D. degree at Jefferson Medical College of Philadelphia in 1919 and was Resident Physician, Butler Hospital, Providence, R. I., from 1921 until 1926. Dr. Wyatt then practiced in Lillington, N. C., from 1926 until 1949, gradually limiting his practice. He was on the Associate Staff of Highsmith Hospital, Fayetteville, N. C., 1931–39. He was an active member of the Harnett County Medical Society and had served as Secretary and President. He was interested in the medical history of North Carolina and prepared several monographs on the early physicians of the state. He served in the Army from 1942 to 1946, when he was retired as a Lieutenant Colonel.

Dr. Wyatt was not an Internist, in the modern sense. He was a pioneer because he returned to the area where he was well known, established a general practice, and then educated his patients as to the need for specialist consultation and care. Many of his patients went to Raleigh to consult him after his retirement.

WILLIAM T. RAINEY, M.D., F.A.C.P.

ABSTRACT OF MINUTES OF THE BOARD OF REGENTS

PHILADELPHIA, PA.

NOVEMBER 15, 1953

The autumn meeting of the Board of Regents convened at the College Headquarters, Philadelphia, Pa., at 9:00 a.m., Sunday, November 15, 1953, with President LeRoy H. Sloan presiding and Mr. E. R. Loveland acting as Secretary, and with the following in attendance:

LeRoy H. Sloan	*President*
Cyrus C. Sturgis	*President-Elect*
George F. Strong	*First Vice President*
Alex. M. Burgess, Sr.	*Second Vice President*
William C. Chaney	*Third Vice President*
William D. Stroud	*Treasurer*
Richard A. Kern	*Secretary-General*
Marion A. Blankenhorn	
Asa L. Lincoln	
Walter L. Palmer	
Wallace M. Yater	
Edward L. Bortz	
Herbert K. Detweiler	
Harold H. Jones	
Howard P. Lewis	
Dwight L. Wilbur	
Philip S. Hench	
Chester S. Keefer	
T. Grier Miller	
Maurice C. Pincoffs	*Editor, "Annals of Internal Medicine"*
Thomas M. McMillan	*Chairman, Committee on Postgraduate Courses*
George Morris Piersol	*Chairman, Committee on Credentials*
Howard Wakefield	*General Chairman, 35th Annual Session*
John C. Leonard	*Committeeman and Governor for Connecticut*
Lemuel C. McGee	*Representative, American Foundation of Occupational Health and Governor for Delaware*

The only absentees were Dr. J. Owsley Manier, Dr. George H. Lathrope, Dr. Eugene B. Ferris and Dr. Charles A. Doan, Chairman of the Board of Governors.

The Secretary read abstracted Minutes of the last meetings of the Board of Regents, held at Atlantic City, April, 1953, and they were approved as read.

The Secretary then presented numerous communications, including:

(1) The appointment by President Sloan of Dr. Cyrus C. Sturgis as representative of the College on a Committee of the American College of Surgeons to supply advice on matters of hospital staff professional performance;

(2) The appointment by President Sloan of Dr. Clyde W. Holland, College Governor for the Maritime Provinces, as official representative of the College at the St. Francis Xavier University Centenary at Antigonish, N. S., September 1–2, 1953;

(3) Appointment by President Sloan of Dr. Josiah J. Moore, F.A.C.P., Chicago, as official observer at the Seventh General Assembly of the World Medical Association at The Hague, August 31-September 5, 1953;

(4) Appointment by President Sloan of Dr. Leon Jacobson, F.A.C.P., Chicago, to serve as an advisory member to the Committee on Cancer of the American College of Surgeons;
(5) Announcement that President Sloan and First Vice President George F. Strong officially attended the annual meeting of the Royal College of Physicians and Surgeons of Canada, Montreal, October 30–31, 1953;
(6) Report by Dr. Robert F. Loeb, F.A.C.P., New York, N. Y., who is official representative of the College in the Division of Medicine, National Research Council;
(7) Announcement of the gift of $109.95, representing refunded travel expenses to the 1953 Annual Session of the College, by Dr. Jose Bisbe, Acting Governor for Cuba at the 34th Annual Session, to be deposited in the College's Postgraduate Course Fund;
(8) An announcement of the extension of the Research Fellowship and Latin-American Fellowship Programs to Cuba, Puerto Rico and Mexico, beginning in 1954;
(9) A suggestion from President Sloan concerning invitations to the Annual Session social affairs of previous important contributors to the College, including the wives of some distinguished former Officers who are now deceased;
(10) A report from Dr. Asa L. Lincoln, Regent, confirming that "a voluntary non-profit, professional membership organization does not come under the enforcement and jurisdiction of the New York State Commission on Discrimination." This applies purely to membership. It is, therefore, entirely legal for the College to include on its proposal form questions relating to race and religion;
(11) A letter of resignation as a Regent and as a member of the Committee on Credentials from Dr. George H. Lathrope, due to illness;
(12) A letter of resignation as a Regent and as a member of the Committee on Credentials from Dr. J. Owsley Manier, due to illness.

On motion duly seconded and carried, the resignations of Doctors Lathrope and Manier, as members of the Committee on Credentials, were accepted, but both men shall remain as members of the Board of Regents. It was suggested that it would be appropriate for the Chair, at his discretion, to appoint two new members of the Committee on Credentials to fill these vacancies—Dr. Lathrope's unexpired term to the spring of 1956; Dr. Manier's unexpired term to the spring of 1955.

Dr. Richard A. Kern, Secretary-General, presented the following report:

"Since the last meeting of this Board, the College has lost by death 2 Masters, 48 Fellows and 7 Associates, as follows: (read list of names)

"Since the last meeting of this Board, thirteen additional Fellows have become Life Members, making a grand total of 1,146, of whom 120 are deceased, leaving a balance of 1,026. The additions to Life Membership include: (read list of names)

"Dr. Roger I. Lee, M.A.C.P., at the request of the President, has submitted the following memorial to Dr. Reginald Fitz, to be spread upon the Minutes of this meeting:

REGINALD FITZ

1885–1953

"When Reginald Fitz died his bibliography consisted of over one hundred eighty items. He was for years a member of the Council on Medical Education and Hospitals of the American Medical Association. Likewise, he was a member of a similar committee of the Massachusetts Medical Society. Naturally enough, when certification boards were set up in the specialties, Dr. Fitz was found on the Board of Internal Medicine. Having served for nearly two years in World War I, it

seemed obvious that he should be Chairman of a Board for Selective Service in World War II. Dr. Fitz served on the staff of the Massachusetts General Hospital, Boston, of the Johns Hopkins Hospital, Baltimore, of the Peter Bent Brigham Hospital, Boston, of the Rockefeller Hospital, New York, at the Mayo Clinic, Rochester, Minn., and of the Evans Memorial, Boston. Dr. Fitz was President of the Suffolk District Medical Society, President of the Massachusetts Medical Society. He was Governor, Regent, President and then Regent of the American College of Physicians, and in 1953 was made a Master of the College.

"Reginald Fitz was a teacher of Medicine directly and indirectly all his professional life. As he grew older, his interests turned more and more towards the History of Medicine. He became Lecturer on the History of Medicine at the Harvard Medical School. He was Assistant Dean in the same school and was the University Marshal of Harvard. Dr. Fitz was always a lover of books. He vitalized the Library of the Harvard Medical School and was a trustee of the Boston Medical Library and was on the Advisory Committee of the Library of the Surgeons General. But Dr. Fitz's interests were not restricted to fixed channels, and he was on the Library Committee of the Town of Brookline where he lived. For some years, until his death, he was a Trustee of Wellesley College. And one more note, while omitting many, is that he was for years a Trustee of the Parkins Institute for the Blind and for several years President of the Trustees.

"Reginald Fitz was primarily an idealist, never a visionary. He was a rare combination of gentleness and enthusiasm. He combined intellectual capacity with a willingness to work hard in any capacity. He did not know how to make enemies, but he had a genius for making friends. He was lovable and all who knew him loved him."

Out of respect for those who had died, including two past Presidents and three past Governors, the Board stood for a moment of silent tribute.

The report of the Secretary-General was accepted.

Dr. Alex. M. Burgess presented the following report on the Joint Commission on Accreditation of Hospitals, Dr. Burgess being one of the Commissioners of the College:

"Mr. President, Officers and Regents of the College: Your representatives on the Joint Commission on Accreditation of Hospitals present their report on the activities of the Commission since its spring meeting on April 19, 1953. A report covering the activities of the Commission up to and including that meeting was presented to this body at the Atlantic City Session of the College. The present communication will include reference to the publication of Standards for Hospital Accreditation, which is available in pamphlet form, and a copy of which is appended to this report. (Attachment A.) A general summary of the field work of the Commission, carried out by its inspectors, will be taken up and the figures as to the results in terms of full, provisional and non-accreditation of the hospitals visited will be presented. Finally, the question of the employment of an inspector by the College, as a major contribution to the work of the Commission, will be discussed and the recommendation of your representatives will be stated.

"The 'Standards for Hospital Accreditation' is published by the Commission in pamphlet form. It incorporates the standards previously promulgated by the American College of Surgeons, with certain modifications and amplifications which have been made by the Commission. The requirements, which are listed, are divided into two groups—those that are 'required' and those that are 'contingent.' The required standards are those which 'are held to be absolute prerequisites to accreditation'—that is, they are essential to all hospitals, large or small. The contingent standards are desirable but are not considered absolutely essential. To quote from the publication: 'Whether they must be met is contingent on the type, size and organization of the

hospital and its financial resources.' Standards are set forth under three main headings: (1) Administrative (including the physical plant); (2) Medical Staff and (3) Nursing Department.

"The field work of the Commission, carried out by the twenty-three inspectors, consists of the determination as to whether the hospitals of the United States and Canada, which desire accreditation, are complying with these standards. It is the plan of the Commission to inspect every hospital once in three years. In the case of each hospital inspection, the report is reviewed by the Director and the final verdict confirmed by the Commission. A hospital may receive full accreditation, partial or no accreditation. In the case of a verdict of partial accreditation, or no accreditation, or where the rating of the inspector has been changed by the Director, the deficiencies are listed and the hospital is informed. Monthly reports are rendered to each commissioner, who then sends in his approval and comments, if any, by mail. The Advisory Committee is empowered to act with the Director in case it is necessary to accomplish immediate cancellation of the approval of any hospital, because of the discovery of a situation judged to be dangerous to patients.

"The following is a summary of the field work of the Commission from its beginning in January, 1953, through October 15:

"*Total* number of hospitals surveyed	952
Full accreditation	719
Provisional accreditation	146
No accreditation	85
Action deferred	2

Changes from previous status

"Upgrade —Provisional to Full accreditation	62
"Upgrade No accreditation to Full accreditation	10
"Upgrade No accreditation to Provisional accreditation	10
"Downgrade—Full to Provisional accreditation	86
"Downgrade Full to no accreditation	24
"Downgrade Provisional to no accreditation	15

"In taking up the question of the employment of an inspector by the College, your attention is first directed to the following facts: There are, at present, twenty-three inspectors who are furnished to the Commission by three of the Member Organizations. The American College of Surgeons furnishes five, the American Hospital Association five and the American Medical Association nine. It is understood that the Canadian Medical Association is planning to furnish an inspector. It seems reasonable to conclude that, to participate fully in the work of the Commission, each Member Organization should contribute at least one inspector.

"The cost to the Member Organization of maintaining one inspector is estimated at $15,000.00 a year. It has been agreed that the starting salary shall be $8,000.00.

"It is to be noted that the surveys, which such an inspector carries out, will be general in nature, just as are the surveys of all the other inspectors. He would not be directly responsible for a study of internships and residencies, as these are carried out by the Council on Medical Education and Hospitals of the AMA. It is worth remembering, however, that the inspectors maintained by the AMA do have a dual function and render a separate report of their studies of internships and residencies to the Council. In the same way, the inspectors furnished by the College of Surgeons carry on a survey of the work in cancer detection and treatment, in addition to their work for the Commission. Therefore, we believe that any inspector whom we employ, who will, it is anticipated, be an internist, could well give special attention to medical educational programs, internships, residencies, fellowships and research

activities, and could render a separate report to the College and to the Board of Internal Medicine, which would be of considerable value. It is to be hoped that such an inspector could be recruited from among the Fellows or Associates of the College.

"In conclusion, your representatives on the Commission present the following recommendation:

"It is recommended that the Board of Regents approve the plan of maintaining one inspector for the field work of the Joint Commission on the Accreditation of Hospitals under conditions of employment similar to those which apply to the inspectors now in the field; and that it take such steps as it decides are practical to accomplish the recruitment of such an inspector."

. . . The adoption of the report was moved and seconded, and opened for discussion, in which it was brought out that an inspector provided by the College would be responsible directly to the Commission; that the $15,000.00 required to finance the inspector would cover his salary and traveling expenses; that the total cost to the College for its share of the Commission's operating expenses and for the special inspector would be approximately $30,750.00. Dr. Herbert K. Detweiler proposed the suggestion that the approval of hospitals is a very important function, that there should be some responsibility of the American Board of Internal Medicine and the College and that the College should think over whether it should not have a committee on approval of hospitals, particularly from the standpoint of residency training.

. . . At this point the motion was put and carried. . . .

Dr. Howard Wakefield, Chairman, made the following report on the work of the Residency Review Committee:

"The Residency Review Committee consists of two members from the American Board of Internal Medicine, two members from the Council on Medical Education and Hospitals of the American Medical Association and two members from the American College of Physicians, with Dr. Edward H. Leveroos of the AMA Council ex officio.

"The three main objectives of the Committee are: (1) development of standards for residency programs in Internal Medicine, acceptable to these three organizations; (2) evaluation on a recurring basis of residency programs in Internal Medicine in relation to these standards; (3) development of a list of approved residency programs which meet these standards, such lists to include the number of years for which each program is accredited.

"The Committee presently meets on the average of twice a year—one meeting just before the Congress on Medical Education and Hospitals and one in conjunction with the Annual Session of the American Medical Association. We are still studying the objectives and requirements, and have a subcommittee, consisting of Dr. Thomas M. Durant and Dr. Francis C. Wood, working on revisions. The AMA inspectors, under Dr. Leveroos, have done an enormous job in the last year in a hospital survey on the recurring basis idea, and I think they have reviewed more than six hundred programs in Internal Medicine in this country.

"Functioning between the two meetings a year is an ad hoc committee, which was established to make a preliminary evaluation of residency programs for the full Committee. This ad hoc committee works hard and thoroughly evaluates each situation before approval is granted. I feel that the work of the Residency Review Committee is being well and effectively conducted."

Dr. Asa L. Lincoln, Chairman of the Committee on Public Relations, presented a report covering the matter of publicity at the Annual Sessions of the College; approval of the Manual on General Practice Departments in Hospitals, as published by the American Academy of General Practice; a recommendation approving of the principle of requiring medical experience and training equivalent to board certification in making hospital appointments, according to the requirements of the Joint Com-

mission on Accreditation of Hospitals; the obvious discrimination by Blue Shield against internists, in that the present setup is largely beneficial to surgeons, rather than to internists, the Committee recommending that the President of the American College of Physicians appoint a committee, selected on a national basis, to meet as soon as possible and to make recommendations to the Board of Regents at the next Annual Session in Chicago, this committee being urged to make every effort to meet representatives of the Blue Cross Program in an attempt to overcome these apparent inequities; approval of the program of the Chicago Museum of Medical Science, an organization devoted to collecting and lending all types and forms of medical teaching aids, with the exception of literature; a recommendation not to make a grant by the College to the Coöperative Research Foundation, because of programs already sponsored by the College; the dismissal of disciplinary action against a Fellow accused of improper publicity; the reference to the Council on Physical Medicine and Rehabilitation of the American Medical Association a communication concerning standardization of hypodermic syringes and needles; a recommendation permitting full-time medical teachers holding the rank of Assistant Professor or lower to attend the Annual Sessions of the College at half the current Guest Fee, or $12.50; and a recommendation that a committee be authorized to seek a conference, perhaps during April in Chicago, with medical members of the Advisory Board of the American Foundation of Occupational Health to consider ways and means for the formation of a joint commission (a) for the support of improved standards in industrial medicine, occupational health and industrial hygiene, and (b) for the consideration of accreditation of such services within industry.

By resolution regularly adopted, the report and recommendations of the Committee on Public Relations were approved.

Dr. William D. Stroud, Treasurer, Representative on the American Council on Rheumatic Fever and Chairman of the House Committee, presented the following reports:

"The Treasurer's Report is supplementary to that of the Committee on Finance. That Committee will report on the investment of surplus funds, any changes recommended for the present portfolio and related subjects. The present security holdings of the College are as follows:

Current Cash Value (entire portfolio)	*Cost or Book Value (entire portfolio)*	*Appreciation*
$1,052,657.00	$932,311.06	$120,345.94

"The annual cash income from securities on our present holding basis is estimated by our investment counselor as $44,989.00, with an average yield of 4.27%. This compares with 4.71% for 1952 and 4.53% for 1951.

"Close contact is maintained with our investment counselors, Drexel & Co., we obtain regular analyses of our accounts from them, and we have their representatives meet with us at the autumn meeting of the Committee on Finance each year.

"This is a report of the representatives of the American College of Physicians on the American Council on Rheumatic Fever. Dr. Currier McEwen has asked me to report for him.

"As you may remember, the College appropriated $1,000.00 on April 1, 1944, to be contributed in whole or in part when their work got underway and the need for same was reported through the College representatives; the money was turned over to the Council during 1946. As a result, the College has been represented on the Council ever since. As time goes on, the relationship of the American Council to the American Heart Association has become clearer, and the Council is now functioning with increasing effectiveness as a component part of the American Heart Association without, at the same time, losing its identity.

"At the present time the Committee on Educational Policy of the Council is reviewing all of the publications of the American Heart Association dealing with rheumatic fever and congenital heart disease which have accumulated over the years, with a view to deciding which are still up to date and whether some of the present ones can be merged and whether any new ones need to be prepared. Other committees are exploring other features of the Council's work.

"The Council on Rheumatic Fever, under its Committee on Criteria of Standards of Care, undertook a coöperative study on rheumatic fever in eight hospital centers in the United States and seven hospital centers in the United Kingdom. The object of this study was a comparison of the efficacy of salicylates, ACTH and Cortisone. A preliminary report was given in 1952 at a meeting of the American Rheumatism Association. The final statistical analysis is now being prepared and promises to give not only the result with regard to the usefulness of these drugs, but also very favorable information on the history of rheumatic fever."

Dr. Stroud's House Committee report referred particularly to operations of the College Headquarters, equipment, and matters of that character. His reports were unanimously accepted by resolution.

Dr. George Morris Piersol, Chairman, presented a detailed report on the work of the Committee on Credentials. Among the chief responsibilities of the Committee had been the review of 356 proposals for Associateship and 152 proposals for Fellowship. Growing out of the recommendations of the Committee, 280 candidates were elected to Associateship and 112 candidates were elected to Fellowship. The names have been published in a previous issue of this Journal, but a summary of the action taken appears below:

Candidates for ASSOCIATESHIP		
Recommended for Election	273	
Fellowship Candidates recommended for election first to Associateship	7*	280
Deferred		74
Associate Candidates recommended for Direct election to Fellowship		2
Rejected		7
		363
Less: Direct Fellowship candidates recommended for Associateship		7*
		356
Candidates for FELLOWSHIP		
Recommended for Advancement to Fellowship	95	
Recommended for election to Direct Fellowship	17	112
Recommended for election first to Associateship		7
Deferred		31
Rejected		2
		152

The subject of granting Honorary Fellowships to physicians in India and elsewhere, outside of North America, was brought up for discussion. It was emphasized that Honorary Fellowships thus far have been restricted to rather distinguished individuals who have been invited to address the Annual Session or Annual Convocation of the College. No action was taken to change this precedent.

A report was received through Dr. George F. Strong, Chairman, from a Committee of the Board of Regents to study proposed changes in the Annual Convocation Ceremony, the original suggestions emanating from the Board of Governors. Dr. Strong's report, in part, was as follows:

"(1) We recommend that the President, at the Convocation, should give possibly a five-minute charge to the newly inducted Fellows, but that his Presidential Address be given at one of the General Sessions, probably just prior to the intermission on Tuesday or Wednesday afternoon, when he would command the largest possible audience, and that this address be of approximately twenty minutes in length;

"(2) The announcement concerning the Brower Scholars, the Research Fellows and the Latin-American Fellows be made at the Annual Business Meeting on Thursday afternoon; the names to appear in the Convocation program and all of these men to be part of the Convocation Procession, but to be seated in reserved seats in the audience;

"(3) The Committee believes that the only important consideration concerning the Convocation Orator is that he be an appropriate and accomplished speaker. It does not think it wise to specify that he should be non-medical or non-scientific. It does not make any difference what his field of activity is, so long as he is an accomplished speaker.

The Committee further recommends that the honorarium be increased up to $500.00 Putting a generous stipend on this oration will help to attract the type of person the College wants;

"(4) As to the length of citations for the Phillips and Bruce Medalists and the Stengel Diplomate, the Committee feels that the citations as at present are excellent;

"(5) The hours for the Pre-Convocation Assembly and Convocation Ceremony: The Governors wish to move this forward—Pre-Convocation Assembly from 7:45 o'clock to 8:30 o'clock, and the Convocation Ceremony to 9:00 o'clock.

The Committee believes that if you make it 9:00 o'clock for the Convocation, that is late for the audience and we would be apt to lose our audience, if the program should start so late. We tried, therefore, to balance these two ideas, and we make the suggestion that the Pre-Convocation Assembly should include all platform guests—members of the Convocation Procession, newly inducted Fellows, Brower Scholars, Research Fellows and Latin-American Fellows.

"(6) Size and constituency of the platform party: At Atlantic City there were 102 people on the platform.

The recommendation of this Committee is that the platform party consist of the Officers, Regents, Guest Speaker, recipients of Awards and Medals, and any honored guests; that is, guests from other Colleges or other organizations. This would be a group of about thirty to thirty-three, depending upon, for instance, the number of Masterships awarded;

"(7) Academic costume: I have felt for a long time that if we are a College and if we are conferring degrees, our Convocation should have something of an academic atmosphere.

It is recommended for the platform party that academic dress be worn, the College to provide the cap and gown and the individual, where he has a hood, to provide that himself. As a small corollary of this suggestion, men sitting in the front row would not have to bring white ties and tails, which is a factor of some consideration for those who travel by air.

As a final consideration, the Committee believes that the President of the College should have a distinctive academic costume that might take the form of a distinctive gown. There are several suggestions:

"(a) That a distinctive, dignified gown be designed, embodying the College colors, and should be academic in its pattern;

"(b) Another thought that instead of a distinctive gown, the same purpose might be served by having a special hood, to be worn with an ordinary cap and grown, the hood to be distinctive of the American College;

"(c) Still another suggestion is that the President wear the ordinary academic robe, his own hood, but that he have a distinctive cap."

After extended discussion, the following action was taken:

(1) The honorarium to the Convocational Orator was approved up to the maximum of $500.00;

(2) Citations of Medalists shall remain as they are, except too much background is to be avoided;

(3) That no reception or cocktail party previous to the Convocation Assembly be held;

(4) That a reception to the new members elected since the last Annual Session be conducted on Tuesday night as a reception and dinner, at the invitation of the Board of Governors to the new members from their individual states, and be attended by the Officers, Regents and Governors;

(5) That at the Chicago Session in April, 1954, there shall be a combined reception and dinner to Officers, Regents and Governors of the College with their wives. The Committee was authorized to bring in also a very few special guests;

(6) Due to inadequacy of the platform, the recommendation that Governors and various types of fellows and scholars be seated in a special area in front of the newly inducted Fellows, rather than on the stage; these individuals, however shall be in the Convocation Procession;

(7) The matter of academic gown was referred for further investigation by the Executive Secretary through appropriate authorities.

Dr. T. Grier Miller, Chairman of the Committee on Membership, reviewed a previous survey made of membership status of members on faculties of medical schools, with relation to membership in the College. The Committee expressed the opinion that more information should be obtained, particularly from those medical schools who failed to supply either adequate or no information. The Committee made the observation that the extension of the Associate term in the College to ten years, initiated a year and a half ago, had led to a reduced number of proposals for advancement to Fellowship. With this trend continuing, the number of Associates will steadily increase and may readily lead to embarrassing failures to attain Fellowship. The Committee further suggested that possibly if the College made all members permanent, either as Members or Fellows, less antagonism and misunderstanding would arise and the prestige of membership would be enhanced. The Committee's report suggested that in case of such a plan being adopted, it would be necessary to redefine the qualifications for membership.

No action was taken, other than to approve the recommendation of the Committee on Membership that their survey be continued, as suggested. The detailed report of the Committee, however, was referred to the Board of Governors for information and further consideration.

Dr. Thomas M. McMillan, Chairman of the Committee on Postgraduate Courses, made an extended report on the courses concluded during 1953, presented the schedule

of courses recommended for the spring of 1954 and a tentative schedule for the autumn of 1954 (these are not recorded here, because they have been published elsewhere in this journal, either during the past month or the current month). The recommendations presented were approved by the Board of Regents.

Dr. Walter L. Palmer, Chairman of the Editorial Board of the Annals of Internal Medicine, in his report pointed out that the responsibility of the new Editorial Board is to make such recommendations to the Board of Regents as it may consider appropriate and to confer with the Editor of the Annals of Internal Medicine and the Executive Secretary of the College, with respect to such problems as may arise. The personnel of this Editorial Board consists of Doctors David P. Barr, O. H. Perry Pepper, Alex. M. Burgess, Sr., Howard P. Lewis and Walter L. Palmer, Chairman. Dr. Palmer's report covered matters of circulation, finances, change in the paper stock of the journal, a new cover design and numerous other matters. Growing out of recommendations of the Committee, the Board of Regents approved the following:

(1) The Executive Secretary was authorized, through the College printers, to accept orders for reprints from others than authors at an appropriate price, provided the permission of the author has been obtained and provided further that adequate assurance is given that the reprints will be distributed in a dignified and ethical manner.
The specific resolution was "reprints of scientific articles that have appeared in the 'Annals of Internal Medicine' may be furnished to individuals or firms for distribution to physicians who have requested such reprints, under the following conditions:

(a) Written permission of the author or authors must be obtained and any restrictions imposed by him must be observed;
(b) Such reprints must be sent to the requesting physicians as received, with no additional printing or stamping of any sort. They may be accompanied by a slip bearing the compliments of the sender, but not by samples or advertising material;
(c) Copies of reprints will be made and furnished under the supervision of the Executive Office of the College, and a charge to cover their reproduction may be made. The making of copies of reprints by other means is not authorized."

(2) That soon after the completion of Volume 40 of the "Annals," June, 1954, a Cumulative Index be prepared and distributed free of cost, on request, to all members of the College and to all subscribing libraries. Other subscribers may obtain the index at a nominal cost fee. A tentative appropriation for this purpose was made of $1,000.00 for the Editor's Office and $5,000.00 for the Executive Secretary's Office;
(3) The Editor and the Executive Secretary were requested to publish only a moderate condensation, or abstract. of Minutes of the Board of Regents and of the Board of Governors in the future;
(4) The News Notes Section, at an appropriate time, shall be removed from the journal and published as a special news bulletin to be distributed only to members of the College.

Dr. Walter L. Palmer, Chairman, presented a report on the American Board of Internal Medicine, announcing that Dr. John S. Lawrence, F.A.C.P., Los Angeles, was elected as successor to Dr. William B. Porter, F.A.C.P., Richmond, for a term of three years, beginning July 1, 1953; that 1,770 candidates took the written examination of the Board in October, 1953, this examination being given in seventy-two different centers all over the world, including Arabia and Japan; oral examinations in 1953 had numbered 670; the final oral was scheduled to be held in Chicago

during December, 1953, for 240 candidates, bringing the total number examined orally in 1953 to about 910; up to date, 8,404 physicians had been certified by the Board.

Dr. George Morris Piersol, Chairman, presented the report for the Committee on Advertisements and Commercial Exhibits, observing that paid advertising in the "Annals" for 1953 would be 704 3/4 pages, an increase of 10.7% over 1952, and that the gross income from advertising would be approximately $74,000.00; he prophesied that the volume of advertising would be further increased in 1954. He announced changes in the advertising rates, which shall become effective January 1, 1954, representing an increase of about 16%, whereas the circulation had increased over 26% since the previous rates were adopted. The Committee reiterated its stand in not approving advertising on the outside covers of the journal. The report also contained details of a new point system in the assignment of exhibit space at the Annual Session, the new plan recognizing prior exhibits and prior advertising.

Dr. Cyrus C. Sturgis made an extended report for the Committee on Fellowships and Awards, giving the details of two meetings of the Committee, one at Ann Arbor on June 20, 1953, and one at Philadelphia on November 13, 1953. In brief, the terms of three of the Latin-American Fellows were extended; programs and reports on seventeen Latin-American Fellows selected in 1952 were presented; the applications of nine new Latin-American Fellows had previously been approved to start July 1, 1953, said candidates being already in the Orientation Course at Cornell University; arrangements had been made for the introduction of Latin-American Fellowships in Cuba and Puerto Rico; follow-up reports were received from previous fellows who had concluded their programs and returned to their homelands; the Committee had obtained, through the Executive Committee of the Board of Regents, approval of the recipients of the John Phillips Memorial and the James D. Bruce Memorial Awards for 1954; Latin-American Fellows now pursuing the Orientation Course were individually interviewed and plans laid for their continued training under preceptors in their particular fields; a list of five Latin-American Fellows with records of their terms of fellowship and to whom Certificates have been issued was recorded; reports on current Latin-American Fellows who are working under preceptors were received; the Kellogg Foundation, since 1949, has expended nearly $200,000.00 on the American College of Physicians—Latin-American Fellowship project; in this period of time, there have been 15 fellows from Chile, 9 from Mexico, 6 from Brazil, 4 each from Peru, Paraguay and Colombia, 2 each from Argentina and Costa Rica and 1 each from El Salvador, Guatemala, Uruguay and Venezuela; 7 Research Fellows of the College are currently at work (their names and programs were outlined).

From a list of 16 applicants for Research Fellowships for 1954–55, the following were selected and an appropriation of $20,000.00 was approved:

"1. *Dr. Robert Shields Abernathy*
Age, 30; a graduate of Duke University School of Medicine, 1949; to work under Dr. Wesley W. Spink, University Hospitals, Minneapolis, Minn., on studies on the pathogenesis of brucellosis along two general lines: (1) rôle of the reticuloendothelial system; (2) rôle of brucella endotoxins; $3,500.00.

2. *Dr. Leon Cander*
Age, 27; a graduate of Temple University School of Medicine, 1951; to work under Dr. Julius H. Comroe, Jr., in the Department of Physiology and Pharmacology, University of Pennsylvania Graduate School of Medicine, on clinical physiology, with emphasis on cardiopulmonary physiology and its application to problems in internal medicine; $3,500.00.

3. *Dr. Margaret Ann Hunt*
Age, 27; a graduate of Washington University School of Medicine, 1951; to work under Dr. Nathan B. Talbot, Massachusetts General Hospital, Boston, Mass., on homeostatic aspects of the care of patients with advanced nephritis; $3,000.00.

4. *Dr. Harry Thurman McPherson*
   Age, 27; a graduate of Duke University School of Medicine, 1948; to work under Dr. Frank J. Engel, Duke Hospital, Durham, N. C., on a quantitative study of ketone metabolism in the human by utilizing the technique of hepatic vein catheterization; $3,000.00.
5. *Dr. Donald Hermann Walters*
   Age, 32; a graduate of University of Wisconsin Medical School, 1950; to work under Dr. A. K. Solomon, Biophysical Laboratory, Harvard Medical School, Boston, Mass., to investigate the effect of calcium and magnesium on the sodium and potassium transport in the human erythrocyte; $3,500.00.
6. *Dr. Joseph Anthony Wilber*
   Age, 28; a graduate of Harvard Medical School, 1952; to work under Dr. Eugene B. Ferris and Dr. Albert A. Brust, Grady Hospital (Emory University School of Medicine), Atlanta, Ga., to study the rôle of the autonomic nervous system in regulating the "responsiveness of the blood vessels" to circulating pressor agents in man; $3,500.00.

The following candidate, *Dr. Donald Hermann Walters*, was selected from the above group to be designated as the "Alfred Stengel Research Fellow," on account of his outstanding qualifications.

Out of a group of 31 applications for the A. Blaine Brower Traveling Scholarships, the Committee had unanimously selected Dr. Richard N. Frohner, of Great Falls, Mont., and Dr. Carroll M. Leevy, of Jersey City, N. J., as the 1954 recipients.

An offer from the Medical Director of Mead Johnson and Company to provide to the American College of Physicians $3,000.00 annually to cover three awards of $1,000.00 each per annum to interns or residents (preferably the latter) in internal medicine was accepted, machinery to be set up by which the College Governor for each territory would nominate one candidate, the Committee on Fellowships and Awards to make the final selection.

The Committee on Fellowships and Awards was authorized to investigate further the matter of the establishment of a loan fund for men in residency training and to confer with the Finance Committee, a report to be made at the Chicago Annual Session.

Dr. A. B. Brower, Chairman, presented a report on behalf of the Committee on Insurance. The Committee expressed satisfaction with the work of Messrs. McCormack and Claypoole, who operate the Association Service Office for the College Group Plans of Health and Accident and Malpractice Insurance. The following summary statistics were reported:

Health and Accident Plan

Total Applications		3,263
Certificates Outstanding		3,063
Applications Cancelled	37	
Applications Pending	53	
Future Date	84	
	174	

Premiums received to date—$434,900.83.

Claims

Notifications received	173
Total Payments made	$44,309.55
Semi-Annual bills not paid	48
Amount of Premiums due	$ 3,572.20

Malpractice Plan

Total Applications received		528
Applications Cancelled	22	
Applications Pending	7	
Applications Future Date	42	
	71	
Certificates Outstanding		457
Premiums Collected		$26,766.47
Claims		None

The Committee announced that new premium rates for the Malpractice Insurance will shortly go into effect, lowering the rates in many of the states, markedly in the higher brackets of coverage.

The report disclosed that the Executive Secretary had checked with the first 117 claimants for benefits under the Health and Accident Plan, and the Committee expressed gratification that there was practically 100% satisfaction and marked enthusiasm by the members.

Dr. Wallace M. Yater, Chairman, presented the report on the Alfred Stengel Memorial Award Committee, presented 4 nominees and, by secret ballot, one was chosen, his name to be announced and the award to be presented at the 1954 Convocation at Chicago.

Dr. Harold H. Jones, Chairman, made the report for the Committee on Constitution and By-Laws, recommending that the Board of Regents adopt a resolution, first, to the effect that it shall not be compulsory for the President to deliver his Presidential Address at the Convocation, and, second, shall approve of an amendment to the By-Laws, Article XII, Annual Convocation, last sentence: "A Presidential Address will be delivered on, *or before*, this occasion." These resolutions were duly adopted and provide that the amendment be presented for action by the Fellows and Masters of the College at the next Annual Business Meeting.

On recommendation of this Committee, no amendment to the By-Laws was recommended, for the present, to provide for representation on the Board of Governors by all of the Canadian Public Services. It was agreed that the head of each Canadian Public Service, Army, Navy, Department of Health and Welfare and the Department of Veterans Affairs, be consulted to determine if such representation is desired.

Dr. Edward L. Bortz, Chairman, presented the report of the Committee on Masterships. The report included the nomination of 5 candidates and brief biographies of each were read. The Board of Regents, by unanimous resolution, elected the following 5 candidates to Mastership, for induction at the Convocation at the next Annual Session:

Dr. Walter L. Bierring, Des Moines, Iowa
Dr. Robert A. Cooke, New York, N. Y.
Dr. Egerton L. Crispin, Los Angeles, Calif.
Dr. James S. McLester, Birmingham, Ala.
Dr. Hugh J. Morgan, Nashville, Tenn.

On recommendation of the Committee, a resolution was adopted providing that each autumn Governors of the College shall be polled for the purpose of obtaining their opinions regarding Fellows of the College in their jurisdiction who in their opinion are worthy candidates for Mastership in the College and that their reasons and their nominations be made available to the Committee on Masterships prior to its autumn meeting.

Dr. Marion A. Blankenhorn, Chairman, made the report for the Committee on Educational Policy, and expressed as one purpose of the Committee, the formulation of opinions and recommendations to the Program Committee of current and future

meetings, particularly through the use of a questionnaire. Such a questionnaire had been used at the conclusion of the last Annual Session and distributed among 271 members in attendance at that Session. The Committee had devised a new questionnaire, which it felt less ambiguous and more practical, and recommended that 300 copies be distributed at the Chicago Annual Session through the Board of Governors (a minimum of three to each Governor; more to Governors in largely populated areas), individual Governors being given the responsibility to collect the returns and to transmit them to the Executive Secretary for summarization. The Committee also recommended that "a suggestion page" be used in the official program, said page being headed "The Committee on Educational Policy asks you to suggest new and different devices to be used at the Annual Session." By resolution the Regents approved of the Committee's suggested questionnaire in substance; also that the suggestion page be added to the Annual Session Program.

A further suggestion of the Committee on Educational Policy included the compilation of a directory of the continuous weekly programs of medical activities in various cities, this directory to be available to members on request. No specific action was taken, but this matter was referred back to the Committee for further consideration.

Dr. Edward L. Bortz reported as Chairman of a temporary Committee on Medical Films. The Committee had discussed the possibility of the College underwriting a motion picture having to do with audio visual methods of teaching or a film depicting the history of the College. The Committee pointed out the difficulties and expense of such an undertaking, and, after general discussion, a resolution was adopted that no action be taken.

The Executive Secretary, Mr. Loveland, reported in some detail on Regional Meetings of the College held during 1953, giving the schedule and attendance. The program of Regional Meetings is becoming more important and more popular, with increasing attendance each year. He reported further to the Regents on a matter referred by the Regents to him, dealing with the designing of some form of recognition to past Officers, past Regents and past Governors of the College. The Governors' Committee on this subject had submitted one final suggestion, namely, a small card to be engrossed, showing the individual's office and dates thereof, this card to be inserted within the Fellowship Certificate frame. Mr. Loveland presented two forms of such engrossed cards and also a small plaque in the form of a certificate. The Board of Regents did not approve of any of the samples presented, feeling them somewhat lacking in practicability and propriety, and directed the Executive Secretary to continue his efforts to arrive at some other form, such as a small, formal certificate.

In concluding his report, the Executive Secretary recommended the appointment by the Board of Regents of a temporary Administrative Committee, to study the current administrative needs of the Central Office. The Board of Regents unanimously approved same and authorized the President to make appointments and to authorize prompt action (President Sloan later appointed Dr. T. Grier Miller, Chairman, Dr. G. M. Piersol, Dr. R. A. Kern and Dr. Wallace M. Yater).

President LeRoy H. Sloan and General Chairman Howard Wakefield reported on the arrangements for their respective programs of the 1954 Annual Session—General Sessions and Morning Symposia by President Sloan; Panels, Hospital Clinics, Clinical-Pathological Conferences, TV Clinics, Entertainment, etc., by General Chairman Wakefield.

(In view of the fact that the program will have been published by the time these Minutes are published, highlights referred to by the Program Committee are herein omitted.)

It was agreed that Dr. Thomas M. Durant, who will be the General Chairman of the Philadelphia Annual Session in 1955, should be invited to participate in the general round-up meeting of Committees for the Chicago Annual Session.

Dr. A. B. Brower, Chairman, presented the report of the Committee on Finance, pointing out that the Committee had conferred with its investment counselors, as it does regularly, before making recommendations to the Regents for purchase or sale of securities. Dr. Brower registered with the Board of Regents all security transactions that had been consummated since the previous meeting of the Board, and the Board of Regents, by resolution, approved such transactions, with particular emphasis on those transactions for the Endowment Fund. Thereupon he presented a list of recommendations made by the investment counselors and approved by the Committee, providing for the sale of certain securities and the purchase of others. He reported the current rate of income on the entire portfolio is 4.27%. He distributed detailed operating statements prepared by the Executive Office covering 1953 and budget proposals for 1954. The operating statements and the budget proposals were carefully and fully discussed, as were also three-year comparative statements regarding the cost of the Annual Sessions and regarding the publication of the "Annals of Internal Medicine." By resolution, the Board of Regents approved the 1954 budgets, covering an estimated income of $372,600.00, estimated expenditures of $320,764.16, leaving an estimated balance of $51,835.84. Included within the above budget was an item of $15,000.00 to cover the salary and expenses of a hospital inspector for the American College of Physicians, to be working under the Joint Commission on Accreditation of Hospitals; also an appropriation of $1,500.00 added to the budget for 1953 for the designing and erection of a College display booth of modern, dignified design, with color transparencies of the College Headquarters and with panels depicting its chief activities and purposes.

Dr. Brower then presented duplicated copies of a survey and analysis of the cost of paying travel expenses of speakers and clinicians on the Annual Session program, as directed by the Board of Regents on April 14, 1953. He pointed out that the custom in the past has been to pay the round trip, first-class train fare, $7.50 per day while traveling and $15.00 per day for the day or days on which a non-member speaker appears on the program of General Sessions or Morning Lectures. At the 1953 Session this amounted only to $691.39, although at some previous Sessions the amount had been between $2,000.00 and $3,000.00. The survey disclosed that if the travel expenses and the per diem allowance were made also to members of the College who are full-time men, it would add $3,200.00, and if extended also to part-time members on the program, it would add another $2,100.00, or if all speakers, whether members of the College or not, who appear on the General Sessions and Morning Symposia programs were allowed their expenses, it would add $5,300.00 over and above present costs. If this same arrangement were done for all members appearing on the Clinics, Panels, Clinical-Pathological Conferences and TV Clinics, it would add another $20,000.00. Combining the above figures, if the College were to pay the travel expenses and per diem allowances to all speakers, all panelists and all clinicians, the cost would be approximately $26,000.00.

After extended discussion, a resolution was adopted not to depart from the present plan at this time in regard to paying travel expenses for speakers at the Annual Sessions of the College.

A resolution was adopted, however, providing that non-members appearing on the program of General Sessions and Morning Symposia in the future shall be allowed the round trip, first-class railroad fare, plus expenses for meals and hotels to the limit of $7.50 per day en route and $25.00 for the day or days on which they appear on the program.

Dr. Wallace M. Yater announced that friends of the Executive Secretary, Mr. Loveland, had arranged for a portrait of him to be painted, for presentation to the American College of Physicians and hung permanently in the College Headquarters at the time of his retirement as an official of the College. By resolution, the Board of Regents agreed officially to accept the portrait, continued a special Committee, consisting of Dr. A. B. Brower, Dr. T. Grier Miller, Dr. Wallace M. Yater, Chairman, and Dr. LeRoy H. Sloan, ex officio, until the portrait has been completed, for the purpose of holding the funds and for making necessary arrangements; and agreed that at the conclusion of the business connected with the painting of the portrait, the residue of funds shall be turned over to the College and be designated as "a special fund for the purpose of acquiring and preserving paintings, drawings or photographs of members or officials of the College," to be used at the discretion of the Board of Regents; and finally that upon completion of the portrait of Mr. Loveland it shall be appropriately framed, insured against damage and theft and presented to Mr. Loveland to keep in his possession, if he is agreeable, until his retirement as an official of the College. Dr. Philip S. Hench suggested that if enough money had been raised in honor of Mr. Loveland, he thought small copies could be made at small cost and presented to his family and friends.

Dr. Yater then brought up the matter of the continuation of the official History of the College. The first edition, published in 1940 under the Historianship of the late Dr. William Gerry Morgan, covered the first twenty-five years, 1915–40. He pointed out that in 1955 there will have been fifteen more years of history that have transpired, and expressed the opinion that the History should be kept up to date by those who have lived through the period, rather than to wait until every one is dead who knows what has been going on. He moved that the Executive Committee of the College select a member of the College to be Historian for the period 1941–55, the appointee to be allowed to enlist the aid of any members of the College or of the Headquarters Staff whom he may desire, and that as soon as possible after 1955 the history for this period be published in book form. The motion was seconded, put and duly carried.

President Sloan announced that the Schering Corporation had agreed to provide funds to underwrite the expenses of the President of the Royal College of Physicians of London as a guest at our 1954 Annual Session; also he expressed the wish to invite another foreign guest for whom he had adequate budget provisions. The Regents, by resolution, approved of both items.

Adjournment.

Attest: E. R. Loveland,
Secretary

TENTATIVE PROGRAM
THE AMERICAN COLLEGE OF PHYSICIANS

Thirty-fifth Annual Session

CHICAGO, ILL.

April 5–9, 1954

GENERAL SESSIONS, SYMPOSIA AND LECTURES

LeRoy H. Sloan, Chicago, Ill., President

GENERAL CHAIRMAN

Howard Wakefield, Chicago, Ill.

Assistants:

Eliot E. Foltz
Raymond M. Galt
Robert P. Gilbert
Edwin N. Irons
Leon O. Jacobson
Edward A. Newman

COMMITTEE ON ARRANGEMENTS

Howard Wakefield, Chairman

Howard B. Carroll
Lowell T. Coggeshall
G. Karl Fenn
George A. Hellmuth
Edwin F. Hirsch
Edwin N. Irons
Frank B. Kelly
Mrs. Walter L. Palmer
Walter S. Priest
Richard H. Young

COMMITTEE ON AUDITORIUM

Edwin N. Irons, Chairman

George V. Byfield
Eliot E. Foltz
Raymond M. Galt
Robert P. Gilbert
Lester A. Nalefski
Edward A. Newman
Jerome T. Paul

COMMITTEE ON HOSPITAL CLINICS

Lowell T. Coggeshall, Chairman

Wright R. Adams, Billings Hospital
Howard L. Alt, Passavant Memorial Hospital
Donald H. Atlas, Mount Sinai Hospital
Lyle A. Baker, Veterans Administration Hospital (Hines)
Fred E. Ball, Jr., St. Luke's Hospital
Harry F. Dowling, Research and Educational Hospital
Richard V. Ebert, Veterans Administration Hospital (Research Center)
Ford K. Hick, Research and Educational Hospital
Franklin A. Kyser, Evanston Hospital
Gilbert H. Marquardt, Wesley Memorial Hospital
George F. O'Brien, Mercy Hospital

Mitchell A. Spellberg, Michael Reese Hospital
Frederick Steigmann, Cook County Hospital
George W. Stuppy, Presbyterian Hospital

COMMITTEE ON CLINICAL PATHOLOGICAL CONFERENCES

Edwin F. Hirsch, Chairman

Israel Davidsohn
Ralph E. Dolkart
Gertrude M. Engbring
Joseph B. Kirsner
Samuel A. Levinson
Hans Popper
Norman B. Roberg
Lowell D. Snorf

COMMITTEE ON ENTERTAINMENT

Walter S. Priest, Chairman

Stuyvesant Butler
Jacob W. Fischer
Hugh A. Flack
Charles S. Gilbert
Robert J. Hasterlik
Mrs. Edwin F. Hirsch
Martin M. Kirshen
Howard A. Lindberg
C. Phillip Miller
Theodore Z. Polley
William K. Scupham
Samuel G. Taylor, III
William H. Wehrmacher

COMMITTEE ON HOTELS AND TRANSPORTATION

George A. Hellmuth, Chairman

George M. Cummins, Jr.
Robert N. Hedges
Donald E. O'Brien
Ralph W. Trimmer
George C. Turnbull
Willard L. Wood

COMMITTEE ON PANEL DISCUSSIONS

G. Karl Fenn, Chairman

S. Howard Armstrong, Jr.
Richard B. Capps
Arthur R. Colwell, Sr.
Frederick W. Fitz
Robert M. Kark
Henry T. Ricketts
Edward F. Rosenberg
Henry L. Schmitz
Irving E. Steck
Willard O. Thompson

COMMITTEE ON PEDIATRICS

Gerald M. Cline, Chairman

Julius H. Hess
Archibald L. Hoyne

COMMITTEE ON PUBLICITY

Howard B. Carroll, Chairman

Evan M. Barton
Albert Carriere
William F. Cernock
Nathan S. Davis
Francis L. Foran
Earle Gray
Grant H. Laing
Louis R. Limarzi
Arthur E. Mahle
Max M. Montgomery
Carl O. Rinder
David H. Rosenberg
Steven O. Schwartz
Theodore R. Van Dellen
George E. Wakerlin

Advisory:

Effie Alley
Roy Gibbons
Robert Kleckner
Arthur Snider

COMMITTEE ON TELEVISED CLINICS

Frank B. Kelly, Chairman

Arthur Bernstein
James A. Campbell
Thomas J. Coogan
Robert H. Ebert
Stanley C. W. Fahlstrom
Edmund F. Foley
Leo L. Hardt
Leon O. Jacobson
Louis N. Katz
Robert C. Levy
Chauncey C. Maher
Paul S. Rhoads

Advisory:

Kendall A. Elsom
Donald J. Hart
Lewis Lang

MEDICAL DEAN'S COMMITTEE OF CHICAGO MEDICAL SCHOOLS

Richard H. Young, Chairman

Granville A. Bennett
Lowell T. Coggeshall
Francis J. Mullin
John F. Sheehan

COMMITTEE ON LADIES' ENTERTAINMENT

Mrs. LeRoy H. Sloan, Honorary Chairman
Mrs. Walter L. Palmer, General Chairman
Mrs. Fred E. Ball, Jr., Vice Chairman

Mrs. Thomas J. Coogan, Adviser
Mrs. Joseph B. Kirsner, Secretary
Mrs. Frank B. Kelly, Treasurer
Mrs. Wright Adams, Assistant Treasurer

Committee Chairmen

Registration:
Mrs. Howard B. Carroll
Mrs. James H. Hutton, Assistant
Mrs. Chauncey C. Maher, Information

Fashion Show Luncheon:
Mrs. Henry L. Schmitz
Mrs. Clifford J. Barborka, Assistant

Kungsholm Luncheon and Opera:
Mrs. Robert N. Hedges

Tours:
Mrs. Edwin N. Irons
Mrs. Richard B. Capps, Museum of Science and Industry
Mrs. Eliot E. Foltz, Donnelley's and Field's
Mrs. Raymond M. Galt, Swift and Company (Thursday)
Mrs. Henry T. Ricketts, Swift and Company (Wednesday)

Hospitality Day:
Mrs. Charles H. Drenckhahn
Mrs. Gilbert H. Marquardt
Mrs. George W. Stuppy

Art Institute Lecture and Tea:
Mrs. C. Phillip Miller

Invitations:
Mrs. Grant H. Laing

Programs:
Mrs. Howard Wakefield

General Committee

Mrs. Howard L. Alt
Mrs. Donald H. Atlas
Mrs. Lyle A. Baker
Mrs. James A. Campbell
Mrs. Lowell T. Coggeshall
Mrs. Arthur R. Colwell, Sr.
Mrs. Harry F. Dowling
Mrs. Lester R. Dragstedt
Mrs. G. Karl Fenn
Mrs. George A. Hellmuth
Mrs. Edwin F. Hirsch
Mrs. Leon O. Jacobson
Mrs. Franklin A. Kyser
Mrs. J. Roscoe Miller
Mrs. Edward A. Newman
Mrs. George F. O'Brien
Mrs. Walter S. Priest
Mrs. Paul S. Rhoads
Mrs. Edward F. Rosenberg
Mrs. Lowell D. Snorf
Mrs. Mitchell A. Spellberg
Mrs. Frederick Steigmann
Mrs. Willard O. Thompson
Mrs. George E. Wakerlin

Mrs. Richard H. Young

INVITATION

You are most cordially invited to attend and to participate in the 35th Annual Session of the American College of Physicians, to be held April 5 to 9, 1954, in Chicago, Illinois.

There are many reasons why it is most fitting that our 35th Annual Meeting should be held in Chicago which has, throughout the years, been host to so many medical groups and distinguished physicians. This great medical center has numerous outstanding hospitals and five medical schools—The Chicago Medical School, The University of Chicago School of Medicine, The University of Illinois College of Medicine, The Stritch School of Medicine of Loyola University and Northwestern University Medical School. Chicago is also the home of a dozen internationally known medical organizations including: The American Medical Association, The American College of Surgeons, The Association of American Medical Colleges, The American Hospital Association, and the Chicago Medical Society (the second largest medical society in the United States).

Every member of our College is fully cognizant of the broadening benefits and the mental stimulation to be derived from our meetings. The purpose of this invitation is not, however, entirely medical. Chicago has much to offer to the visitor in addition to its excellent medical facilities. It is a respected center of learning and commerce, with world famous universities and great markets. Among its most noteworthy scientific contributions is the first self-sustaining chain reaction which started the controlled release of nuclear energy, and gives promise of eventually serving every field of science and industry. Chicago is the home of the finest museums and art galleries. Music lovers are inspired by the Chicago Symphony Orchestra under the able leadership of its new conductor, Fritz Reiner. A special concert will be given by this orchestra for the members of the College and their guests on Monday evening, April 5.

The City of Chicago has been a gracious host to millions of visitors because it is the hub of various transportation facilities and therefore readily accessible to all parts of this hemisphere. It has ample and satisfactory hotel accommodations for all who wish to attend our meeting. Wives and daughters will enjoy the program arranged for their entertainment; as well as visits to museums, art galleries, department stores and specialty shops for which Chicago is famous.

An interesting and outstanding scientific program has been arranged which we know will have both educational and inspirational value for all who attend.

WELCOME!

GENERAL INFORMATION

HEADQUARTERS

Registration headquarters, the information bureau, technical exhibits, general sessions, morning lectures, panel discussions, clinical-pathological conferences, televised clinics, meetings of Committees, of the Board of Regents and of the Board of Governors, Convocation, Annual Banquet, as well as hotel headquarters, will be the Conrad Hilton Hotel, Chicago, Ill. The Chicago Symphony Orchestra Concert will be held at Orchestra Hall, 216 S. Michigan Ave., Chicago.

HOTEL ACCOMODATIONS

The following list of hotels, having adequate rooms to accommodate all for this meeting, are situated near the Conrad Hilton Hotel. It will not be necessary to set up a Housing Bureau. Members and guests may utilize the official registration form accompanying the program, or they may write directly, identifying themselves with this Convention, to the hotel of their choice. The hotel reservation form has been devised for use by both the American Heart Association and the American College of Physicians, since the American Heart Association is meeting at the Conrad Hilton Hotel from April 1–4, immediately preceding the meeting of the College. By using this form and making a reservation for the entire period of both Conventions, one may prevent the necessity of having to move from one hotel to another between meetings. Additional copies of the hotel reservation form may be obtained from the Executive Secretary of the College, 4200 Pine Street, Philadelphia 4, Pa.

LIST OF HOTELS

Hotel	Size (Rooms)	For One Person	For Two Persons		Suites
			Double Bed	Twin Beds	
Atlantic 316 S. Clark	400	$4.50–$ 6.00	$ 6.00–$ 7.50	$ 8.00–$ 9.00	$13.50–$15.00
Blackstone S. Michigan and Balbo	376	5.00– 12.00	10.00– 14.00	12.00– 16.00	26.00– 65.00
Congress 520 S. Michigan	1,000	6.00– 12.00	8.50– 15.00	10.50– 15.50	17.50– 35.00
*Conrad Hilton 720 S. Michigan	2,500	5.50– 13.00	10.00– 17.00	10.50– 22.00	22.00– 48.00
Harrison 65 E. Harrison	400	5.00– 7.00	7.00– 9.50	8.50– 10.50	18.50– 24.00
Palmer House 15 E. Monroe	2,242	5.00– 12.75	11.50– 16.25	12.50– 19.00	28.50 and up

* Headquarters.

Who May Register—

(*a*) All members of the American College of Physicians in good standing for 1954.

(*b*) All newly elected members.

(*c*) Graduate medical students pursuing courses in local institutions of Chicago, including residents in Chicago hospitals, without registration fee, **upon presentation of matriculation cards or other evidence of registration at these institutions**; admission to exhibits, general sessions, morning lectures and TV clinics.

(*d*) Members of the staff, including interns, of the Chicago hospitals participating in the program, without registration fee, **upon presentation of proper identification**; admission to exhibits, general sessions, morning lectures and TV clinics (this does not include courtesy staff members).

(*e*) Bona fide hospital residents, regardless of their location in North America, without registration fee, **upon presentation of proper credentials from their hospitals**; admission to exhibits, general sessions, morning lectures, and other program features where facilities are adequate.

(*f*) Members of the Medical Corps of the Army, Navy, Public Health Service, Air Force and Veterans Administration, either of the United States or Canada, without registration fee, **upon presentation of proper credentials.**

(*g*) Qualified physicians who may wish to attend this Session as visitors, sponsored in advance by letter or in person by a member of the College; such physicians shall pay a registration fee of $25.00, and shall be entitled to one year's subscription to the ANNALS OF INTERNAL MEDICINE (in which the proceedings will be published) included within such fee.

(*h*) Full-time medical teachers holding the rank of Assistant Professor or lower, **upon presentation of proper credentials from their medical schools,** shall be entitled to a reduction in the registration fee to $12.50.

The above regulations are essential because of the increasingly large attendance at the Annual Sessions of the College, and the necessity of accommodating members first.

Registration Bureau—While official registration will start on Monday morning, April 5, advance registration of members and exhibitors will be provided for by mail. The Registration Bureau will be set up for advance registration at the Conrad Hilton Hotel on Sunday, April 4, from 2:30 P.M. to 5:00 P.M. The Registration Bureau, located in the lower lobby, Exhibition Floor, of the Conrad Hilton Hotel, will be open throughout the week from 8:45 A.M. to 5:30 P.M.

Advance Registration of Members—In order to facilitate quick registration at the meeting for members of the College, an advance registration form, with directions, will be enclosed with the formal Program to all Fellows and Associates. The success and justification of the plan is wholly dependent upon the co-operation of members, and thus the directions should be carefully noted and the proper forms returned to the Executive Offices of the College long in advance, so that each member's envelope of forms and badge will be ready for him when he calls at the Advance Registration Window. The use of this form will eliminate long lines and delays so frequently encountered at large Conventions. A member, however, should not send in this form unless he is sure he is going to be present.

Registration Blanks for all Panel Discussions and Clinical-Pathological Conferences will be enclosed with the final program to members of the College. Non-members will secure registration blanks at the Registration Bureau during the Session.

Daily Bulletins—A Daily Bulletin of registrations will be published at this meeting.

Bulletin Board for special announcements will be located near the Registration Bureau.

Transportation—Local transportation arrangements are in charge of the Committee on Hotels and Transportation, which will issue information at the meeting. Taxicabs are recommended in connection with the hospital clinics.

The Annual Business Meeting of the College will be held at 2:00 P.M., Thursday, April 8, immediately preceding the afternoon general session. All Masters and Fellows of the College are urged to be present. There will be the election of Officers, Regents and Governors, the annual reports of the Secretary-General, Executive Secretary and Treasurer. Announcements will be made of the Research Fellowship Awards, Latin-American Fellowship Awards and the A. Blaine Brower Traveling Scholarship Awards. The President-Elect, Dr. Cyrus C. Sturgis, Ann Arbor, Mich., will be inducted into office.

BOARD AND COMMITTEE MEETINGS

All meetings will be held at the Conrad Hilton Hotel at times and places indicated. Special meetings will be announced and posted.

A **Reception and Dinner** of the members of the Board of Regents, Board of Governors, Committee Chairmen, distinguished guests, and their wives, will be held Sunday, April 4, at 7:00 P.M., in the Tower Room, Conrad Hilton Hotel. Entertainment will include music and the appearance of Edgar A. Guest, "the People's Poet," humorist, columnist and writer, whose poems appear daily in syndicated papers throughout the country.

Committee on Nominations

(At the call of the Chairman)

Committee on Credentials

Saturday, April 3, 10:00 A.M., Room No. 2, Third Floor

Committee on Membership

Sunday, April 4, 9:15 A.M., Room No. 2, Third Floor

Committee on Fellowships and Awards

Sunday, April 4, 10:00 A.M., Executive Secretary's Office, Room No. 1, Third Floor

Committee on Finance

Sunday, April 4, 11:15 A.M., Executive Secretary's Office, Room No. 1, Third Floor

Joint Meeting: Board of Regents and Board of Governors

Sunday, April 4, 2:00 P.M., Room No. 2, Third Floor

Reference Committee on Blue Shield

Monday, April 5, 8:30 A.M., a breakfast-meeting, private dining Room No. 3, Third Floor

Committee on Educational Policy

Monday, April 5, 10:00 A.M., Executive Secretary's Office, Room No. 1, Third Floor

Committee on Postgraduate Courses

Monday, April 5, 10:00 A.M., Room No. 2, Third Floor

Committee on Public Relations

Monday, April 5, 11:00 A.M., Room No. 2, Third Floor

Editorial Board, Annals of Internal Medicine

Monday, April 5, 11:00 A.M., Executive Secretary's Office, Room No. 1, Third Floor

Inspection, Committee on Technical Exhibits

Monday, April 5, 10:30 A.M., starting from the Executive Secretary's Office, Room No. 1, Third Floor

Meeting, Technical Exhibitors

Monday, April 5, 5:20 P.M., Room No. 2, Third Floor

Meeting, Board of Governors

*Tuesday, April 6, 12:00 M., Room No. 2, Third Floor

Meeting, Board of Regents

*Wednesday, April 7, 12:00 M., Room No. 2, Third Floor

Annual Business Meeting

Thursday, April 8, 2:00 P.M., Grand Ballroom

Meeting, Board of Regents

*Friday, April 9, 12:00 M., Room No. 2, Third Floor

SPECIAL FEATURES

"Seminars in Medicine of Mexico"—A Post-Convention Tour to Mexico City, leaving Chicago, Saturday, April 10, by DC-6 Flagships of the American Airlines; arriving in Mexico City the same evening; scientific sessions at the National Institute of Cardiology on Monday and Wednesday forenoons and at the Hospital de Enfermedades de la Nutricion, arranged by Dr. Ignacio Chavez, F.A.C.P., College Governor for Mexico and Dr. Salvador Zubiran, F.A.C.P. Conducted sight-seeing tours of great interest in and about Mexico City and to Cholula and Puebla are included. For full details, itinerary, costs, etc., consult special bulletin obtainable from the Conductor, Mr. Leon V. Arnold, 36 Washington Square West, New York 11, N. Y.

Concert, Chicago Symphony Orchestra, Monday evening, April 5, 8:15 P.M., Orchestra Hall, 216 S. Michigan Ave., Chicago—Orchestra Hall, which is the permanent home of the Chicago Symphony Orchestra, is between Jackson Boulevard and

* Buffet luncheon served.

Adams Street on Michigan Avenue, and is easily within walking distance of the Conrad Hilton and other Loop hotels. The Committee on Entertainment is gratified to announce this Concert by the great Chicago Symphony Orchestra, under the direction of Fritz Reiner, who is planning a most attractive program for the College members. The citizens of Chicago are devoted to its great Orchestra, and it is a special privilege to have this Orchestra entertain the members of the College at a private Concert. There will be no charge of admission; tickets will be supplied by the Executive Office of the College on request, first come, first served. Members should send in their applications immediately; non-members, duly registered at the Session, may obtain tickets at the A.C.P. Registration Desk at the Conrad Hilton Hotel. Orchestra Hall seats about 2,700. Seats will be reserved only for Officers, Regents, Governors, distinguished guests, and their wives.

A Symphony Concert makes an ideal prologue for a scientific meeting. It will be one of the social highlights of the 35th Annual Session of the College.

Reception and Dinner, tendered by Officers, Regents and Governors of the College to new Associates and Direct Fellows: Conrad Hilton Hotel, Tuesday evening, April 6, 6:30 P.M.—The Governors of the College extend an invitation to all new Associates and Direct Fellows who have been elected on or since April 12, 1953, for the purpose of welcoming them to the College and to provide an opportunity to meet them personally and for them to meet the Officers and Regents of the College, as well as one another. Dr. Walter Biering will give a short talk on "Medical Echoes."

Special invitations will be issued by mail in advance of the Annual Session; it is urgently necessary for the Executive Office to receive acceptances or declinations promptly and in advance.

The Annual Convocation and President's Reception, Wednesday evening, April 7—The Annual Convocation of the College will be held at 8:40 P.M. in the Ballroom of the Conrad Hilton Hotel. All members of the College and their families and the Chicago public who are interested are very cordially invited. Tickets will not be required. All physicians elected Fellows of the College since the 1953 Convocation, and all previously elected Fellows who have not been formally inducted, should be present. Officers, Regents, Governors, distinguished guests on the program and new Fellows to be inducted are requested to assemble in the Normandie Lounge, Second Floor, Conrad Hilton Hotel, at 8:00 P.M., preparatory to the formation of the procession, which will move promptly at 8:40 o'clock.

The Convocation Ceremony will include the induction of the new Fellows, a short charge to the new members by the President, Dr. LeRoy H. Sloan, and the Convocational Oration, "The Past and Future of the Atomic Development," by Dr. Enrico Fermi, distinguished physicist of the Institute of Nuclear Studies of the University of Chicago. The John Phillips Memorial Medal for 1954, the James D. Bruce Memorial Medal for 1954, and the Alfred Stengel Diploma for 1954 will be awarded. Masterships will be conferred upon five distinguished Fellows of the College. As distinguished guests, there will be present the Presidents of the American College of Surgeons, American Medical Association, the Royal College of Physicians and Surgeons of Canada and the Royal College of Physicians of London.

Following the Convocation the audience is requested temporarily to leave the Ballroom while the chairs are removed and arrangements set up for the President's Reception and Ball; dancing from 10:00 P.M. to 1:00 A.M.

The Annual Banquet, Thursday, April 8, 8:00 P.M.—At 7:00 P.M., in the Normandie Lounge of the Conrad Hilton Hotel will be held a "Dutch Treat" Cocktail Party, to which all members and their guests are cordially invited.

The Annual Banquet will follow at 8:00 o'clock in the Grand Ballroom. Dr. Lawrence A. Kimpton, Chancellor of the University of Chicago, will be the speaker of the day, his title, "Medicine and the Educational Process." Dr. Howard Wake-

field, General Chairman of the Session, will be the Toastmaster. A gala occasion, with excellent food, good fellowship and fine entertainment is assured. Table reservations for groups may be arranged in advance. Tickets should be procured at the Registration Bureau on the Exhibition Floor of the Conrad Hilton Hotel by 2.00 P.M., Wednesday, in order that adequate preparations may be concluded by the Committee. Tickets, $9.00 per person.

ENTERTAINMENT OF VISITING WOMEN

The Committee on Ladies' Entertainment in Chicago extends a cordial welcome to the wives and daughters of the members of the American College of Physicians, and hopes that the functions which have been planned will afford a diversity of entertainment and an opportunity for friendly association.

Headquarters for the Ladies' Registration are in the North Assembly Room on the third floor of the Conrad Hilton Hotel, and all tickets may be purchased there.

Certain of the entertainment features are limited in accommodations and, therefore, your cooperation in early registration is requested.

Please wear your badge to all entertainments.

Consult Bulletin Board daily.

Headquarters are in the North Assembly Room on the third floor of the Conrad Hilton Hotel. The registration hours are as follows:

Sunday, April 4.....2:00 P.M. to 5:00 P.M.
Monday, April 5.....9:00 A.M. to 4:00 P.M.
Tuesday, April 6.....9:00 A.M. to 4:00 P.M.
Wednesday, April 7.....9:00 A.M. to 4:00 P.M.
Thursday, April 8.....9:00 A.M. to 12 Noon

Daily Program

Monday, April 5

Hospitality Day—9:00 A.M. to 4:00 P.M. North Assembly Room on the third floor of the Conrad Hilton.

We hope that you will meet your friends here and linger over a cup of coffee. At this time you also will have the opportunity of meeting the wives of the Officers, Regents and Governors who will be hostesses.

2:00 P.M. to 4:00 P.M. Two showings of John Nash Ott's colored movies, "Flowers in Action." North Ball Room, adjoining the Ladies' Headquarters on the third floor of the Conrad Hilton.

8:15 P.M. The Chicago Symphony Orchestra, under the direction of Fritz Reiner. Orchestra Hall, 216 South Michigan Avenue.

Your husbands should procure tickets for the concert through the Central Office of the College or at the Men's Registration Bureau.

Tuesday, April 6

9:45 A.M. to 11:45 A.M. Tour of R. R. Donnelly and Sons Co. Round trip on bus, 75¢.

9:45 A.M. to 11:45 A.M. "Behind the Scenes" at Marshall Field's. Round trip on bus, 75¢.

1:00 P.M. Luncheon in the Crystal Ballroom, Blackstone Hotel, Michigan Avenue and Balbo Drive. Fashion Show by Marshall Field and Co. Tickets, $5.00.

Note: All busses leave from the South Entrance of the Conrad Hilton Hotel on Eighth Street.

Wednesday, April 7

9:45 A.M. Tour of Swift and Co. Luncheon at the Saddle and Sirloin Club, the Stock Yard Inn. Busses leave the Conrad Hilton promptly, and return to the hotel at approximately 1:30 P.M. Total cost, $5.00.

12:00 Noon. Smorgasbord Luncheon at the Kungsholm Restaurant. "La Tosca" in the Miniature Grand Opera Theater. Reservations limited. Luncheon and opera, $3.50. Round trip on bus, $1.00.

8:40 P.M. The Annual Convocation. The President's Reception and Ball. Grand Ballroom, the Conrad Hilton Hotel.

Note: All busses leave from the South Entrance of the Conrad Hilton Hotel on Eighth Street.

Thursday, April 8

9:30 A.M. Trip to the Museum of Science and Industry. Demonstration of the Heart Exhibit. Round trip on bus, $1.00, returning to the Conrad Hilton at approximately 1:30 P.M.

9:45 A.M. Tour of Swift and Co. Luncheon at the Saddle and Sirloin Club, the Stock Yard Inn. Busses leave the Conrad Hilton promptly, and return to the hotel at approximately 1:30 P.M. Reservations limited. Total cost, $5.00.

2:15 P.M. Visit to the Art Institute of Chicago, Michigan Avenue at Adams Street. Brief address by Mr. Daniel Catton Rich, Director of the Institute, Fullerton Hall. Gallery tours and tea. Tickets, $1.50.

7:00 P.M. Cocktail Party. Normandie Lounge.

8:00 P.M. The Annual Banquet of the College. Grand Ballroom, the Conrad Hilton Hotel.

Note: All busses leave from the South Entrance of the Conrad Hilton Hotel on Eighth Street.

Color Televised Clinics—Again through the courtesy of Smith, Kline & French Laboratories, Philadelphia, and the cooperation of Columbia Broadcasting System, the College will present for the fifth year an interesting program of clinics televised in color from St. Luke's Hospital to the Conrad Hilton Hotel, Exhibition Floor, from 9:00 A.M. to 12:30 P.M., daily, Tuesday through Friday.

"Medical Films That Teach"—The Medical Film Guild, of New York City, will present in the Ballroom, following the General Sessions in the afternoons of Monday, Tuesday, Wednesday and Thursday the following timely films produced in color and sound (see program of general sessions):

Rheumatoid Disorders—Pharmacology and Clinical Evaluation of a Modern Therapeutic Agent. Projection time, 35 minutes.

Radioisotopes—Their Application to Humans as Tracer Studies and for Therapeutic Use. Projection time, 32 minutes.

Arterial Insufficiency of the Extremities—Physiology, Diagnosis and Treatment. Projection time, 15 minutes.

Occupational Health Problems—Ranging from the pre-Employment Examination to the Correction of Occupational Hazards in Atomic Energy Installations. Projection time, 42 minutes.

Clinical Pathological Conferences—To fulfill the special interests of many members and to relieve congestion in the afternoon General Sessions, the Program Committee has introduced certain Clinical-Pathological Conferences and Panel Programs in the afternoon, running concurrently with the General Sessions, but not starting until 4:00 P.M.

The Technical Exhibit—The Technical Exhibit will be located on the Exhibition Floor of the Conrad Hilton Hotel, and will be one of the best conducted by the College. The Committee on Exhibits maintains the highest possible standards in the conduct of this Exhibit. Exhibitors are admitted only by invitation. Irrelevant exhibits are eliminated, and only firms which present a group of approved products or services of scientific interest to the internist and allied specialist may exhibit.

Members and guests of the College are encouraged to accord the exhibitors courteous and interested attention. Many thousand dollars are expended by the exhibitors to bring to this College superior displays and up-to-date information concerning pharmaceuticals, equipment, medical books and medical services. The Technical Exhibitors gauge this meeting by the amount of interest shown and the co-operation displayed by the College.

Exhibits will be open from 8:45 A.M. to 5:30 P.M., daily, Monday through Thursday, and from 8:45 A.M. to 12:45 P.M., on Friday. Physicians are urged to use the intermission in the program for inspection of the exhibits, but these intermissions are inadequate for a thorough visit and inspection of the large number of exhibits, and thus physicians are encouraged to spend some additional time in this important part of the meeting.

PARTIAL LIST OF TECHNICAL EXHIBITORS

	Booth
Abbott Laboratories, North Chicago, Ill.	99–100
Alkalol Company, The, Taunton, Mass.	31
W. D. Allison Company, St. Louis, Mo.	118
American Ferment Co., Inc., New York, N. Y.	97
American Hospital Supply Corporation, Evanston, Ill.	61–62
American Journal of Medicine, The, New York, N. Y.	130
Ames Company, Inc., Elkhart, Ind.	11
Appleton-Century-Crofts, Inc., New York, N. Y.	33
Armour Laboratories, The, Chicago, Ill.	53
Association of American University Presses, New York, N. Y.	122
Ayerst, McKenna & Harrison Limited, New York, N. Y.	70–71
W. A. Baum Co., Inc., Copiague, L. I., N. Y.	26
Becton, Dickinson and Company, Rutherford, N. J.	23–24
Bilhuber-Knoll Corp., Orange, N. J.	28
Ernst Bischoff Company, Inc., Ivoryton, Conn.	29
Blakiston Company, Inc., The, New York, N. Y.; Toronto, Can.	115
Borcherdt Malt Extract Company, Chicago, Ill.	21
Bowen & Company, Inc., Bethesda, Md.	20
Brewer & Company, Inc., Worcester, Mass.	76
Burdick Corporation, The, Milton, Wis.	98
Bureau of Medicine and Surgery, U. S. Navy, Washington, D. C.	4
Burroughs Wellcome & Co. (U.S.A.) Inc., Tuckahoe, N. Y.	56
Burton, Parsons & Company, Washington, D. C.	25
Cambridge Instrument Co., Inc., Chicago, Ill.; Philadelphia, Pa.; Cleveland, Ohio; New York, N. Y.	67
Chicago Dietetic Supply House, Inc., The, Chicago, Ill.	3
Chilean Iodine Educational Bureau, Inc., New York, N. Y.	66
Ciba Pharmaceutical Products, Inc., Summit, N. J.	91–112
Clersite Company, Chicago, Ill.	22

	Booth
Warren E. Collins, Inc., Boston, Mass.	101
Coreco Research Corp., New York, N. Y.	120
County Surgical Co., Inc., Brooklyn, N. Y.	107
Curvlite Surgical Products, Div. Mastercraft Plastics Co., Inc., Jamaica, N. Y.	106
Davies, Rose & Company, Limited, Boston, Mass.	12
Desitin Chemical Company, Providence, R. I.	18
Devereux Schools, Devon, Pa.	32
DeVilbiss Company, The, Somerset, Pa.	34
Doho Chemical Corporation, New York, N. Y.	77–78
Duke Laboratories, Inc., Stamford, Conn.	16
Electro-Physical Laboratories, Inc., Stamford, Conn.	123
Fellows Medical Mfg. Co., Inc., New York, N. Y.	111
Fine Chemicals Division, American Cyanamid Company, Princeton, N. J.	124–125
C. B. Fleet Co., Inc., Lynchburg, Va.	60
Geigy Pharmaceuticals, New York, N. Y.	109
General Electric Company, X-Ray Department, Milwaukee, Wis.	13–14
General Foods Corporation, New York, N. Y.	19, 105, 128
Gerber Products Company, Fremont, Mich.	102
Grune & Stratton, Inc., New York, N. Y.	75
Harrower Laboratory, Inc., The, Jersey City, N. J.	110
H. J. Heinz Company, Pittsburgh, Pa.	63
Paul B. Hoeber, Inc., New York, N. Y.	39
Hoffman-La Roche, Nutley, N. J.	10
Hollister-Stier Laboratories, Chicago, Ill.; Philadelphia, Pa.; Los Angeles, Calif.; Spokane, Wash.	64
Horlicks Corporation, Racine, Wis.	121
Hyland Laboratories, Los Angeles, Calif.	17
Irwin, Neisler & Company, Decatur, Ill.	36
Ives-Cameron Company, Inc., New York, N. Y.	119
Joint Commission on Accreditation of Hospitals, Chicago, Ill.	1
Jones Metabolism Equipment Co., Inc.	15
"Junket" Brand Foods, Little Falls, N. Y.	131
Lea & Febiger, Philadelphia, Pa.	93
Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.	85
Eli Lilly and Company, Indianapolis, Ind.	46–47–48
J. B. Lippincott Company, Philadelphia, Pa.	79–80
Little, Brown and Company, Boston, Mass.	103
Macmillan Company, The, New York, N. Y.	57
Massachusetts Indemnity Insurance Company, Boston, Mass.	126
S. E. Massengill Company, Bristol, Tenn.	7

	Booth
Mead Johnson & Company, Evansville, Ind.	42
Medco Products Company, Tulsa, Okla.	94
Medical Bureau, The, Chicago, Ill.	40
Medical Film Guild, Ltd., New York, N. Y.	30
Merck & Co., Inc., Rahway, N. J.	44–45
Wm. S. Merrell Company, The, Cincinnati, Ohio	52
C. V. Mosby Co., The, St. Louis, Mo.	83
National Drug Company, The, Philadelphia, Pa.	81–82
Nepera Chemical Co., Inc., Yonkers, N. Y.	114
O.E.M. Corporation, East Norwalk, Conn.	65
Oxford University Press, Inc., New York, N. Y.	43
Parke, Davis & Company, Detroit, Mich.	41
Pet Milk Company, St. Louis, Mo.	116
Chas. Pfizer & Co., Inc., Brooklyn, N. Y.	51
Pharmaseal Laboratories, Glendale, Calif.	127
Riker Laboratories, Inc., Los Angeles, Calif.	108
A. H. Robins Company, Inc., Richmond, Va.	86
Sanborn Company, Cambridge, Mass.	58–59
Sandoz Chemical Works, Inc., Pharmaceutical Division, New York, N. Y.	84
W. B. Saunders Company, Philadelphia, Pa.	95–96
Schenley Laboratories, Inc., New York, N. Y.	41–A
Schering Corporation, Bloomfield, N. J.	69–90
G. D. Searle & Co., Chicago, Ill.	9
Shampaine Company, St. Louis, Mo.	117
Sharp & Dohme, Inc., Philadelphia, Pa.	49–50
Smith, Kline & French Laboratories, Philadelphia, Pa.	73–74
E. R. Squibb & Sons, Division of Mathieson Chemical Corporation, Long Island City, N. Y.	54–55
Technicon Company, The, New York, N. Y.	37
Upjohn Company, The, Kalamazoo, Mich.	88–89
U. S. Vitamin Corporation, New York, N. Y.	8
Varick Pharmacal Co., Inc., Subsidiary, E. Fougera & Company, New York, N. Y.	5–6
Wallace & Tiernan Company, Inc., Newark, N. J.	27
Warner-Chilcott Laboratories, New York, N. Y.	35
White Laboratories, Inc., Kenilworth, N. J.	68
Williams & Wilkins Company, The, Baltimore, Md.	92
Winthrop-Stearns, Inc., New York, N. Y.	113–132
Woodward Medical Personnel Bureau, Chicago, Ill.	72
Wyeth Laboratories, Philadelphia, Pa.	38
Year Book Publishers, Inc., The, Chicago, Ill.	87

OUTLINE OF THE CHICAGO SESSION

April 5–9, 1954

(All events at the Conrad Hilton Hotel, except Hospital Clinics and Concert)

TIME	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY
	April 5	April 6	April 7	April 8	April 9
9:00 A.M. to 10:20 A.M.	Morning free **Registration, Exhibits, etc.**	Hospital Clinics **Color Televised Clinics**	**Morning Lectures Color Televised Clinics**	Hospital Clinics **Color Televised Clinics**	**Morning Lectures Color Televised Clinics**
10.20 A.M. to 11.00 A.M.		**Intermission**	**Intermission**	**Intermission**	**Intermission**
11:00 A.M. to 12:30 P.M.		Hospital Clinics **Color Televised Clinics Panels (6)**	**Color Televised Clinics Panels (5)**	Hospital Clinics **Color Televised Clinics Panels (5)**	**Color Televised Clinics Panels (6)**
2:00 P.M. to 3:20 P.M.	**1st General Session**	**2nd General Session**	**3rd General Session**	**Annual Business Meeting 4th General Session**	**5th General Session**
3:20 P.M. to 4:00 P.M.	**Intermission**	**Intermission**	**Intermission**	**Intermission**	
4:00 P.M. to 5:00 P.M.	**1st General Session** (Continued)	**2nd General Session** (Continued) **C-P Conference**	**3rd General Session** (Continued) **Panel—Pancreatic Disease C-P Conference**	**C-P Conference**	**C-P Conference** (3:00 to 4:00)
5:00 P.M. to 5:30 P.M.	**Exhibits**	**Exhibits**	**Exhibits**	**Exhibits**	
Evening	**Symphony Concert**	**Reception to New Members**	**Convocation & President's Reception**	**Cocktail Party Annual Banquet**	

GENERAL SESSIONS PROGRAM

Grand Ballroom, Conrad Hilton Hotel

FIRST GENERAL SESSION

Monday Afternoon, April 5, 1954

Presiding Officer

HOWARD WAKEFIELD, F.A.C.P., Chicago, General Chairman

P.M.

2:00 **Invocation:**

The Right Reverend GERALD FRANCIS BURRILL, Bishop of the Episcopal Diocese of Chicago.

Addresses of Welcome:

The Honorable MARTIN H. KENNELLY, Mayor of the City of Chicago.

WALTER C. BORNEMEIER, F.A.C.S., President, Chicago Medical Society.

WILLIS J. POTTS, F.A.C.S., President, Institute of Medicine of Chicago.

RICHARD B. CAPPS, F.A.C.P., President, Chicago Society of Internal Medicine.

RICHARD H. YOUNG, F.A.C.P., Dean, Northwestern University Medical School, on behalf of all five medical schools of Chicago.

Response to Addresses of Welcome:

LEROY H. SLOAN, F.A.C.P., President, The American College of Physicians.

Presiding Officer

President LEROY H. SLOAN, F.A.C.P., Chicago

2:30 **The James D. Bruce Memorial Lecture on Preventive Medicine: Endemic Goiter; A Problem in Preventive Medicine.**

DAVID MARINE, A.M., M.D., D.Sc., F.A.C.P., Rehoboth, Del.

3:00 **Pitfalls and Promise in Cancer Control.**

CORNELIUS P. RHOADS, M.D., D.Sc. (Hon.), F.A.C.P., Director, Sloan-Kettering Institute for Cancer Research, New York.

3:30 INTERMISSION. Visit the Exhibits.

SECTION I*

Presiding Officer

MAURICE C. PINCOFFS, M.A.C.P., Baltimore

4:00 **The Riddle of Sarcoidosis.**

WILLIAM S. MIDDLETON, M.A.C.P., Dean and Professor of Medicine, University of Wisconsin Medical School, Madison.

4:20 **Periarteritis Nodosa: Recognition and Clinical Symptomatology.**

MARION A. BLANKENHORN, F.A.C.P., Professor of Medicine, University of Cincinnati College of Medicine, Cincinnati.

* Note: The General Sessions programs are divided at mid-afternoon into two sections, either section available according to choice.

4:40 **The Pathology of the Collagen Diseases—Periarteritis Nodosa and Disseminated Lupus.**
WILLIAM BOYD, M.D. (by invitation), Professor of Pathology, University of British Columbia, Vancouver.

5:00 ADJOURNMENT.

5:00 **Elective: "Occupational Health Problems."**
Ranging from the pre-employment examination to the correction of occupational hazards in atomic energy installations. A motion picture in color and sound; projection time, 42 minutes.

SECTION II

North Ballroom, Conrad Hilton Hotel

Monday Afternoon, April 5, 1954

Presiding Officer

WILLIAM D. STROUD, F.A.C.P., Philadelphia

P.M.

4:00 **Virtue of Prompt Anticoagulant Therapy in Impending Myocardial Infarction.**
E. STERLING NICHOL, F.A.C.P., Medical Director, Miami Heart Institute; Attending Cardiologist, Jackson Memorial Hospital; Miami.

4:15 **Hormonal Factors in Heart Disease.**
WILHELM RAAB, F.A.C.P., Professor of Experimental Medicine, University of Vermont College of Medicine, Burlington.

4:30 **The Effect of Healed Subacute Bacterial Endocarditis on Cardiac Dynamics. Results of a Ten-year Follow-up.**
WALTER S. PRIEST, F.A.C.P., Associate Professor of Medicine, JACQUES M. SMITH, M.D. (by invitation), Instructor in Medicine, and GERALD R. GRANN, M.D. (by invitation), Associate Professor of Medicine; Northwestern University Medical School, Chicago.

4:45 **Serial Electrocardiographic Study of Two Sequential Myocardial Infarctions.**
CHAUNCEY C. MAHER, F.A.C.P., Associate Professor of Medicine, HUGH A. FLACK (Associate), Instructor in Medicine, and JOHN A. MART, M.D. (by invitation), Instructor in Medicine; Northwestern University Medical School, Chicago.

5:00 ADJOURNMENT.

SECOND GENERAL SESSION

Grand Ballroom, Conrad Hilton Hotel

Tuesday Afternoon, April 6, 1954

Presiding Officer

WILLIAM S. MIDDLETON, M.A.C.P., Madison

P.M.

2:00 **Cervical Spondylosis.**
SIR W. RUSSELL BRAIN, President, Royal College of Physicians of London.

SECTION I

2:30 **The Management of Venous Thrombosis and Its Sequela.**
HARRIS B. SHUMACKER, JR., F.A.C.S. (by invitation), Professor of Surgery, University of Indiana School of Medicine, Indianapolis.

2:55 **Coronary Disease in American Soldiers Killed in Action in Korea.**
WILLIAM F. ENOS (by invitation), Major, M. C., U. S. Army.
Discussant.
WALLACE M. YATER, F.A.C.P., Regent, Washington.

3:20 INTERMISSION, followed by Clinical Pathological Conference in same room, 4:00 to 5:00. (Consult CPC program.)

5:00 **Elective: "Rheumatoid Disorders—Pharmacology and Clinical Evaluation of a Modern Therapeutic Agent."**
A motion picture in color and sound; projection time, 35 minutes.

SECTION II

Tuesday Afternoon, April 6, 1954

North Ballroom, Conrad Hilton Hotel

Presiding Officer

ALEX. M. BURGESS, SR., F.A.C.P., Providence

P.M.
2:30 **Gout—Now Amenable to Control.**
ELMER C. BARTELS, F.A.C.P., Physician, Department of Internal Medicine, Lahey Clinic, Boston.

2:45 **Effect of Protein Anabolic Steroids in Paget's Disease.**
GILBERT S. GORDAN, JR. (Associate), Assistant Professor of Medicine, University of California School of Medicine, San Francisco.

3:00 **Proteinuria Patterns in Differentiation of Renal Disorders.**
S. EDWARD KING, F.A.C.P., Associate Professor of Clinical Medicine, New York University Postgraduate Medical School, New York.

3:20 ADJOURNMENT, followed by Clinical Pathological Conference in Grand Ballroom, 4:00 to 5:00. (Consult CPC program.)

THIRD GENERAL SESSION

Grand Ballroom, Conrad Hilton Hotel

Wednesday Afternoon, April 7, 1954

Presiding Officer

GEORGE F. STRONG, F.A.C.P., Vancouver, B. C.

P.M.
1:45 **The President's Report.**
LEROY H. SLOAN, F.A.C.P., Chicago.

SECTION I

Presiding Officer

JONATHAN C. MEAKINS, M.A.C.P., Montreal

2:00 **The John Phillips Memorial Lecture: Tubular Renal Failure After Shock and in Nephritis.**

DONALD D. VAN SLYKE, Ph.D., Sc.D., M.D. (by invitation), Brookhaven National Laboratory, Upton, N. Y.

2:30 **The Lilly Lecture: Physiological Basis for the Clinical Use of Nor-Adrenaline.**

U. S. VON EULER, M.D. (by invitation), Professor of Physiology, Karolinska Institutet, Stockholm, Sweden.

3:00 **The Clinical Usefulness of ACTH in Liver Disease.**

VICTOR M. SHOROV (Associate), Assistant Professor of Medicine, University of California Medical School, San Francisco.

3:20 INTERMISSION, to be followed by Panel on Pancreatic Disease in same room, 4:00 to 5:00. (Consult Panel program), and by Clinical-Pathological Conference in the Boulevard Room, 4:00 to 5:00. (Consult CPC program.)

5:00 **Elective: "Radioisotopes—Their Application to Humans as Tracer Studies and for Therapeutic Use."**

A motion picture in color and sound; projection time, 32 minutes.

SECTION II

North Ballroom, Conrad Hilton Hotel

Presiding Officer

HERBERT K. DETWEILER, F.A.C.P., Toronto

4:00 **The Internist and Life Insurance.**

HARRY E. UNGERLEIDER, F.A.C.P., Director of Medical Research, Equitable Life Assurance Society of the United States, New York.

4:20 **The Surgical Treatment of Rheumatic Aortic Insufficiency.**

CHARLES P. BAILEY, F.A.C.S. (by invitation), Associate Professor of Thoracic Surgery, Hahnemann Medical College and Hospital of Philadelphia.

4:40 **Survival Value of Mechanical Aids to Breathing. Case Report of Poliomyelitis.**

ALVAN L. BARACH, F.A.C.P., Clinical Professor of Medicine, and GUSTAV J. BECK, M.D. (by invitation), Assistant in Medicine; Columbia University College of Physicians and Surgeons, New York.

5:00 ADJOURNMENT.

ANNUAL CONVOCATION

Wednesday Evening, April 7, 1954

8:40 O'Clock

Grand Ballroom, Conrad Hilton Hotel

LEMUEL C. MCGEE, Marshal

Pre-Convocation Assembly of Fellows to be inducted, Officers, Regents, Governors, Distinguished Guests and Recipients of Awards, Normandie Lounge, second floor, at 8:00 P.M.

All members of the profession and the general public are cordially invited.

1. Processional.
2. The President's Charge to New Fellows of the American College of Physicians.
   LEROY HENDRICK SLOAN.
3. Conferring of Fellowships by the President.
4. Conferring of Masterships by the President.
5. Presentation of the John Phillips Memorial Medal for 1954.
6. Presentation of the James D. Bruce Memorial Medal for 1954.
7. Presentation of the Alfred Stengel Memorial Award for 1954.
8. Convocational Oration: "The Past and Future of the Atomic Development."
   ENRICO FERMI, Professor of Physics, University of Chicago.
9. Recessional.

The President's Reception and Ball will follow at 10:15 o'clock. The audience is requested to vacate the Grand Ballroom temporarily while the room is reset for the Reception and Dancing. A cordial invitation is extended to all members and guests, with their families.

FOURTH GENERAL SESSION

Grand Ballroom, Conrad Hilton Hotel

Thursday Afternoon, April 8, 1954

P.M.

2:00 THE ANNUAL BUSINESS MEETING.

All Fellows and Masters are urged to be present and to participate more actively in the administrative problems of the College. Announcements will be made of the Research Fellowship Awards, Latin-American Fellowship Awards and the A. Blaine Brower Traveling Scholarships. An amendment to the By-Laws will be presented for ratification. Reports will be received from the Secretary-General, Executive Secretary and Treasurer; elections of new Officers, Regents and Governors will take place; President-Elect Cyrus C. Sturgis, of Ann Arbor, Mich., will be inducted as President and will make a brief inaugural address.

SECTION I

Presiding Officer

CHESTER S. KEEFER, F.A.C.P., Boston

2:40 (Title and speaker to be announced)

3:05 **Recurrent Pneumonia in Multiple Myeloma and Some Observations of Immunologic Response.**

HORACE H. ZINNEMAN (Associate), Instructor in Medicine, University of Minnesota Medical School; Chief, Tuberculosis Follow-up Clinic, Veterans Administration Hospital; and WENDELL H. HALL (Associate), Assistant Professor of Medicine and Bacteriology, University of Minnesota Medical School; Minneapolis.

3:20 INTERMISSION, followed by Clinical Pathological Conference in same room, 4:00 to 5:00. (Consult CPC program.)

5:00 **Elective: "Arterial Insufficiency of the Extremities—Physiology, Diagnosis and Treatment."**

A motion picture in color and sound; projection time, 15 minutes.

SECTION II

North Ballroom, Conrad Hilton Hotel

Presiding Officer
RICHARD A. KERN, F.A.C.P., Philadelphia

2:40 **The Influence of Customs on Disease.**

ISADORE SNAPPER, M.D. (by invitation), Director of Medicine and Medical Education, Beth-El Hospital, Brooklyn.

3:05 **North American Blastomycosis—Clinical Forms of the Disease and Treatment with Stilbamidine and 2-Hydroxystilbamidine.**

WHEELAN D. SUTLIFF (Associate), Associate Professor of Medicine, University of Tennessee College of Medicine; Chief of Section, V. A. Medical Teaching Group Hospital; Memphis.

3:20 INTERMISSION, followed by Clinical Pathological Conference in Grand Ballroom, 4:00 to 5:00. (Consult CPC program.)

Thursday Evening, April 8, 1954

7:00 o'Clock

Normandie Lounge, Conrad Hilton Hotel

"DUTCH TREAT" COCKTAIL PARTY

8:00 o'Clock

Grand Ballroom, Conrad Hilton Hotel

THE ANNUAL BANQUET OF THE COLLEGE

Toastmaster:

HOWARD WAKEFIELD, F.A.C.P., Chicago

Address of the Day:

"Medicine and the Educational Process"

LAWRENCE A. KIMPTON, Chancellor of the University of Chicago

Procure tickets at the Registration Bureau, Exhibition Floor, Conrad Hilton Hotel, before 2:00 P.M., Wednesday. Arrangements may be made for table reservations.

FIFTH GENERAL SESSION

Grand Ballroom, Conrad Hilton Hotel

Friday Afternoon, April 9, 1954

Presiding Officer

PHILIP S. HENCH, F.A.C.P., Rochester

P.M.

2:00 **The Search for the Soul.**
PERCIVAL BAILEY, M.D. (by invitation), Distinguished Professor of Neurology and Neurological Surgery, and Clinical Professor of Psychiatry, University of Illinois College of Medicine, Chicago.

2:20 **The Modern Management of Tuberculosis.**
ROBERT A. GOODWIN, JR., F.A.C.P., Assistant Professor of Clinical Medicine, Vanderbilt University School of Medicine; Chief, Tuberculosis Service, Veterans Administration Hospital; Nashville.

2:40 **Electron Microscopy of Early Cytoplasmic Changes Due to Influenza Virus.**
CARL G. HARFORD, M.D. (by invitation), Associate Professor of Medicine, Washington University School of Medicine, St. Louis.

3:00 **Further Observations on Patients with Severe Hypertension Subjected to Adrenal Resection and Sympathectomy.**
WILLIAM A. JEFFERS, F.A.C.P., Associate Professor of Medicine and Member of Robinette Foundation for Study of Cardiovascular Diseases, University of Pennsylvania School of Medicine; HAROLD A. ZINTEL, F.A.C.S. (by invitation), Associate Professor of Surgery, University of Pennsylvania Graduate School of Medicine; A. GORMAN HILLS, M.D. (by invitation), Associate in Medicine, University of Pennsylvania School of Medicine; STEPHEN B. LANGFELD, M.D. (by invitation), Instructor in Medicine, University of Pennsylvania School of Medicine; and CHARLES C. WOLFERTH, F.A.C.P., Emeritus Professor of Medicine, University of Pennsylvania School of Medicine; Philadelphia.

3:20 **The Medical Management of Patients Following Bilateral Adrenalectomy.**
DELBERT M. BERGENSTAL, M.D. (by invitation), Assistant Professor of Medicine, University of Chicago School of Medicine, Chicago.

3:40 **Bronchoscopic Survey of 7,500 Patients.**

GEORGE WALLACE HOLMES, F.A.C.S. (by invitation), Associate in Surgery, Northwestern University Medical School; Attending Thoracic Surgeon, Cook County Hospital; Chicago.

4:00 **New Methods of Surgical Treatment of Degenerative Diseases of the Aorta.**

ORMAND C. JULIAN, F.A.C.S. (by invitation), Assistant Professor of Surgery; WILLIAM S. DYE, M.D. (by invitation), Instructor in Surgery; and WILLIAM J. GROVE, F.A.C.S. (by invitation), Assistant Professor of Surgery; University of Illinois College of Medicine, Chicago.

4:20 **Treatment of Spontaneous (Essential?) Hypertension in Dogs with Renin and Antirenin.**

JEROME B. KATZ, M.D. (by invitation), and GEORGE E. WAKERLIN, F.A.C.P., Professor and Head of the Department of Physiology, University of Illinois College of Medicine, Chicago.

4:40 **The Management of High Blood Pressure in Older Women.**

HOWARD WAKEFIELD, F.A.C.P., Associate in Medicine, Northwestern University Medical School; Chief of Medical Staff, St. Luke's Hospital; Chicago.

5:00 ADJOURNMENT.

MORNING LECTURES AND SYMPOSIA

Tuesday, April 6, 1954

I. SYMPOSIUM ON PEDIATRICS

Boulevard Room, Conrad Hilton Hotel

Presiding Officer

GERALD M. CLINE, F.A.C.P., Bloomington

A.M.

9:00 **Simplicity in the Treatment of Meningitis.**

ARCHIBALD L. HOYNE, F.A.C.P., Professor of Pediatrics, Chicago Medical School; Chief of Staff, Cook County Contagious Hospital; Chicago.

9:20 **The Age of Immunization.**

FRANKLIN H. TOP, F.A.C.P., Professor and Head, Department of Hygiene and Preventive Medicine, State University of Iowa College of Medicine, Iowa City.

9:40 **Rare Complications of Poliomyelitis.**

ALEX J. STEIGMAN, M.D. (by invitation), Professor of Child Health, University of Louisville School of Medicine, Louisville.

10:00 **Acute Infectious Diseases in Pregnancy.**

CONRAD WESSELHOEFT, F.A.C.P., Professor Emeritus of Clinical Medicine, Boston University School of Medicine; Lecturer on Infectious Diseases, Harvard School of Public Health; Boston.

10:20 ADJOURNMENT, followed by Panel Discussion in same room, 11:00 to 12:30. (Consult Panel program.)

Wednesday, April 7, 1954

II. MORNING LECTURES

Grand Ballroom, Conrad Hilton Hotel

Presiding Officer

HUGH J. MORGAN, F.A.C.P., Nashville

A.M.

9:00 **Facts about Cardiac and Non-cardiac Pain.**
ARTHUR M. MASTER, F.A.C.P., Associate Professor of Clinical Medicine, Columbia University College of Physicians and Surgeons, New York.

9:20 **Rehabilitation of the Patient with Coronary Artery Disease.**
JEROME G. KAUFMAN, F.A.C.P., Assistant Professor of Medicine, New York Medical College, Flower and Fifth Avenue Hospitals; Attending Physician, Newark City and Newark Beth Israel Hospitals; and MARVIN C. BECKER (Associate), Assistant in Medicine, Newark City and Newark Beth Israel Hospitals; Newark.

9:40 **Pregnancy Complicated by Heart Disease.**
EDWIN P. MAYNARD, JR., F.A.C.P., Clinical Professor of Medicine, State University of New York College of Medicine at New York City.

10:00 **The Management of Refractory Edema.**
E. HUGH LUCKEY, F.A.C.P., Director, Second (Cornell) Medical Division, Bellevue Hospital, New York.

10:20 ADJOURNMENT, followed by Panel Discussions, 11:00 A.M. to 12:30 P.M. (Consult Panel program.)

III. MORNING LECTURES

North Ballroom, Conrad Hilton Hotel

Presiding Officer

EUGENE B. FERRIS, F.A.C.P., Atlanta

9:00 **Deaths from Hypertension; Analysis of Ten Years' Experience in a Large General Hospital.**
KENNETH A. EVELYN, F.A.C.P., Associate Professor of Medicine and Director of Research Institute of Biophysics, McGill University Faculty of Medicine, Montreal.

9:20 **Emergency Treatment of Apoplexy by Sympathetic Block.**
GEZA DE TAKATS, F.A.C.S., Professor of Surgery, University of Illinois College of Medicine, Chicago.

9:40 **The Problem of Cerebrovascular Disease.**
IRVING S. WRIGHT, F.A.C.P., Professor of Clinical Medicine, Cornell University Medical College, New York.

10:00 **Critical Discussion of the Problems of Cerebrovascular Disease in England and America.**
SIR W. RUSSELL BRAIN, D.M. (Oxon), (by invitation), President, Royal College of Physicians of London.

10:20 ADJOURNMENT, followed by Panel Discussions, 11:00 A.M. to 12:30 P.M. (Consult Panel program.)

Wednesday, April 7, 1954—(Continued)

IV. MORNING LECTURES

Boulevard Room, Conrad Hilton Hotel

Presiding Officer

WILLIAM C. CHANEY, F.A.C.P., Memphis

A.M.

9:00 **The Heart in Acute Glomerulonephritis.**

TIMOTHY R. MURPHY (Associate), Clinical Instructor in Medicine; and FRANCIS D. MURPHY, F.A.C.P., Professor of Medicine and Head of the Department; Marquette University School of Medicine, Milwaukee.

9:15 **The Problem of Cardiac Stress.**

HOWARD A. RUSK, F.A.C.P., Professor and Chairman, Department of Physical Medicine and Rehabilitation, New York University College of Medicine, New York.

9:30 **The Heavy Metal Content of Cardiovascular Structures (Preliminary Report).**

GEORGE C. GRIFFITH, F.A.C.P., Professor of Medicine, and EDWARD M. BUTT, M.D. (by invitation), Professor of Pathology; University of Southern California School of Medicine, Los Angeles.

9:45 **A New Pancreatic Function Test Based on Starch Tolerance.**

THEODORE L. ALTHAUSEN, F.A.C.P., Professor of Medicine and Chairman of Department; and KAHN UYEYAMA, M.D. (by invitation), Assistant Clinical Professor of Medicine; University of California Medical School, San Francisco.

10:00 **Use of Marginal Man Power in Military Service.**

ELMER L. CAVENY (Associate), Captain, (MC), U. S. Navy; Head, Neuropsychiatry Section, Bureau of Medicine and Surgery, Department of the Navy, Washington.

10:20 ADJOURNMENT, followed by Panel Discussions, 11:00 A.M. to 12:30 P.M. (Consult Panel program.)

Thursday, April 8, 1954

V. MORNING LECTURES

Grand Ballroom, Conrad Hilton Hotel

Presiding Officer

EDWARD L. BORTZ, F.A.C.P., Philadelphia

A.M.

9:00 **An Evaluation of the Effect of Choline Inositol on the Clinical Course and Serum Lipids in Patients with Angina Pectoris.**

RAYMOND S. JACKSON (Associate), Associate Professor of Medicine, and CHARLES F. WILKINSON, JR., F.A.C.P., Professor and Chairman, Department of Medicine, New York University Post-Graduate Medical School, New York.

9:20 **Electrocardiographic Diagnosis of Acute Myocardial Ischemia.**

GORDON B. MYERS, F.A.C.P., Professor of Medicine, Wayne University College of Medicine, Detroit.

9:40—**Modern Ballistocardiography.**

BENJAMIN M. BAKER, JR., F.A.C.P., Associate Professor of Medicine, and MARTIN L. SINGEWALD, F.A.C.P., Instructor in Medicine; Johns Hopkins University School of Medicine, Baltimore.

10:00 **Chemotherapy of Leukemia and Related Disorders.**

M. M. WINTROBE, F.A.C.P., Professor of Medicine, University of Utah College of Medicine, Salt Lake City.

10:20 ADJOURNMENT, followed by Panel Discussion in same room, 11:00 A.M. to 12:30 P.M. (Consult Panel program.)

Friday, April 9, 1954

VI. MORNING LECTURES

Grand Ballroom, Conrad Hilton Hotel

Presiding Officer

CYRUS C. STURGIS, F.A.C.P., Ann Arbor

A.M.

9:00 **Late Effects of Internally Deposited Radioactive Materials.**

WILLIAM B. LOONEY, M.D. (by invitation), Lieutenant, (MC), U. S. Naval Reserve, Radioisotope Laboratory, U. S. Naval Hospital, Bethesda, Md.

9:15 **Clinical Research Using Compounds Labeled with Radioactive Carbon and Hydrogen as Tracers.**

GEORGE V. LEROY, M.D. (by invitation), Associate Dean, Division of Biological Sciences, University of Chicago School of Medicine, Chicago.

9:30 **The Evaluation of the Rate of Formation and the Rate of Destruction of Red Blood Cells as Measured to Radioisotopes.**

JOSEPH F. ROSS, F.A.C.P., Associate Professor of Medicine, Boston University School of Medicine, Boston.

9:45 **Radioactive Iodine in Therapy of Hyperthyroidism.**

DWIGHT E. CLARK, F.A.C.S. (by invitation), Professor of Surgery, University of Chicago School of Medicine, Chicago.

10:00 **Application of Artificial Radioisotopes in Interstitial Therapy (Gold and Cobalt).**

WILLIAM G. MYERS, F.A.C.P., J. F. Stone Research Associate Professor of Medical Biophysics, Ohio State University College of Medicine, Columbus.

10:20 ADJOURNMENT, followed by Panel Discussion on same subject in Boulevard Room, 11:00 A.M. to 12:30 P.M. (Consult Panel program.)

VII. MORNING LECTURES

North Ballroom, Conrad Hilton Hotel

Presiding Officer

ASA L. LINCOLN, F.A.C.P., New York

9:00 The Effect of Synthetic Thyroxine and Its Analogues on the Heart.

PAUL STARR, F.A.C.P., Professor of Medicine and Chairman, Department of Medicine, University of Southern California School of Medicine, Los Angeles.

9:20 The Endocrine Disturbances and Their Dietetic Background in the Undernourished of Mexico.

SALVADOR ZUBIRAN, F.A.C.P., Professor of Internal Medicine, Universidad Nacional Facultad de Medicina de Mexico and Graduate School of Medicine, Universidad Nacional de Mexico, Mexico, D. F.

9:40 The Pattern of Stress and Strain in Disease.

J. S. L. BROWNE, F.A.C.P., Professor of Medicine and Chairman of the Department, McGill University Faculty of Medicine.

10:00 Studies of the Hyperlipemia in Diabetes and Other Disorders.

EDWIN F. HIRSCH, F.A.C.P., Research Associate and Associate Professor of Pathology, University of Chicago School of Medicine; Director, Henry Baird Favill Laboratory, St. Luke's Hospital; Chicago.

10:20 ADJOURNMENT, followed by Panel Discussions, 11:00 A.M. to 12:30 P.M. (Consult Panel program.)

PANEL DISCUSSIONS

Topics of intimate interest and practical value to all members of the College have been chosen. Qualified men have been selected as Moderators and Panelists. All Panels are scheduled from Tuesday through Friday from 11:00 A.M. to 12:30 P.M., except that on Wednesday there will be a Panel on Pancreatic Disease from 4:00 P.M. to 5:00 P.M., running concurrently with the last half of the Third General Session.

Applications for tickets to all Panels may be made in advance by members on a regular application form which will accompany the program. Tickets will also be available at the Registration Bureau, Conrad Hilton Hotel. NON-MEMBERS may not register by mail, but should secure their tickets directly at the meeting.

Applicants may submit in writing three weeks before the Session, through the Executive Secretary of the College, any questions concerning any phase of the subjects listed. Moderators and Panel personnel will answer those questions which they feel are applicable to the subject under discussion, and will answer as many questions as time permits. Furthermore, Moderators will devote, if time permits, thirty-five to forty minutes to questions submitted from the floor.

THE PANEL PROGRAM

Tuesday April 6 11:00 A.M. to 12:30 P.M.	**Liver Disease** Moderator John R. Neefe Philadelphia *Richard B. Capps Chicago *Paul Gyorgy Philadelphia *Franklin M. Haager New York *Hans Popper Chicago Victor M. Sborov San Francisco	**Recent Theories Concerning Arteriosclerosis** Moderator *Louis N. Katz Chicago *William Dock New York Smith Freeman Chicago Raymond S. Jackson New York Ruth Pick	**Peripheral Arterial Disease** Moderator *Hugh Montgomery Philadelphia *David I. Abramson Chicago *Nelson W. Barker Rochester Geza de Takats Chicago Harris B. Shumacker, Jr. Indianapolis	**Recent Developments in the Treatment of Cancer** Moderator *C. P. Rhoads New York Delbert M. Bergenstal Chicago *Leon O. Jacobson Chicago *Rulon W. Rawson New York	**The Internist Looks at Backache** Moderator Charley J. Smyth Denver Fremont Chandler Chicago *Howard P. Lewis Portland *Edward F. Rosenberg Chicago Adrien VerBrugghen Chicago	**Pediatrics** Moderator *Julius H. Hess Chicago *H. William Elghammer Chicago *Benjamin M. Gasul Chicago *Archibald L. Hoyne Chicago Alex J. Steigman Louisville *Franklin H. Top Iowa City *Conrad Wesselhoeft Boston
Wednesday April 7 11:00 A.M. to 12:30 P.M.	**Treatment of Hypertension** Moderator *Robert W. Wilkins Boston *Jose J. Centurion Havana *Eugene B. Ferris Atlanta *Thomas Findley New Orleans Keith S. Grimson Durham *George E. Wakerlin Chicago	**The Treatment of Peptic Ulcer** Moderator *Sara M. Jordan Boston *T. L. Althausen San Francisco *Lester R. Dragstedt Chicago *Walter L. Palmer Chicago Waltman Walters Rochester	**Chemotherapy and Antibiotics** Moderator *Wesley W. Spink Minneapolis *M. A. Blankenhorn Cincinnati Paul A. Bunn Syracuse *Harry F. Dowling Chicago *Paul S. Rhoads Chicago	**Emotional Factors in Disease** Moderator *Edward Weiss Philadelphia Roy Grinker Chicago *William C. Menninger Topeka *Stewart G. Wolf, Jr. Oklahoma City	**Diabetes** Moderator *Henry T. Ricketts Chicago *Arthur R. Colwell, Sr. Chicago *Jerome W. Conn Ann Arbor *Randall G. Sprague Rochester	
4:00 P.M. to 5:00 P.M.	**Pancreatic Disease** Moderator *Henry L. Bockus Philadelphia Warren H. Cole Chicago *Mandred W. Comfort Rochester *Henry T. Ricketts Chicago Waltman Walters Rochester Pathologist Archie H. Baggenstoss Rochester Physiologist Wm. V. Whitehorn Chicago					

*F.A.C.P.

THE PANEL PROGRAM

Thursday April 8 11:00 A.M. to 12:30 P.M.	**Clinical Hematology** Moderator *Carl V. Moore St. Louis *William Dameshek Boston *Charles A. Doan Columbus *Karl Singer Chicago *Maxwell M. Wintrobe Salt Lake City	**The Medical Aspects of Pre- and Postoperative Care** Moderator *Hugh J. Morgan Nashville *Alex. M. Burgess Providence *Richard A. Kern Philadelphia *Roy W. Scott Cleveland *Charles T. Stone Galveston	**Electrocardiography and Vectorcardiography** Moderator *Franklin D. Johnston Ann Arbor Robert P. Grant Atlanta *Richard Langendorf Chicago Oglesby Paul Chicago Brendan P. Phibbs Chicago	**The Cause and Treatment of Edema** Moderator *E. Hugh Luckey New York *S. Howard Armstrong Chicago *Thomas M. Durant Philadelphia Elliot V. Newman Nashville *Eugene A. Stead, Jr. Durham	**Unusual Infectious Diseases** Moderator *John W. Brown Madison *Samuel J. Hoffman Chicago *Archibald L. Hoyne Chicago *Paul S. Rhoads Chicago Isadore Snapper New York	
Friday April 9 11:00 A.M. to 12:30 P.M.	**The Treatment of Coronary Disease** Moderator *Herrman L. Blumgart Boston *A. Carlton Ernstene Cleveland *George C. Griffith Los Angeles *Robert L. King Seattle *Robert L. Levy New York	**The Use and Abuse of Androgens and Estrogens** Moderator *Willard O. Thompson Chicago *J. S. L. Browne Montreal Allan T. Kenyon Chicago Leo T. Samuels	**Rheumatic Diseases** Moderator *Philip S. Hench Rochester *Joseph J. Bunim Bethesda *Richard H. Freyberg New York *Currier McEwen New York *Edward F. Rosenberg Chicago *Irving E. Steck Chicago	**Value of Cardiac Catheterization in Diagnosis** Moderator James A. Campbell Chicago Richard J. Bing Birmingham Robert L. Grissom Omaha James V. Warren Durham	**Problems in Viral Disease** Moderator Albert Milzer *Paul B. Beeson New Haven Carl G. Harford St. Louis Albert B. Sabin Cincinnati	**Use of Radioactive Material in Internal Medicine** Moderator *Leon O. Jacobson Chicago Dwight E. Clark Chicago George V. LeRoy Chicago William B. Looney Bethesda *William G. Myers Columbus *Joseph F. Ross Boston

*F.A.C.P.

CLINICAL–PATHOLOGICAL CONFERENCES

Clinical-Pathological Conferences are scheduled Tuesday, Wednesday and Thursday from 4:00 P.M. to 5:00 P.M. and on Friday from 3:00 P.M. to 4:00 P.M., often running concurrently with other afternoon program features. The clinical protocols of interesting medical cases will be discussed by the participants who are expected to make the correct diagnoses. The postmortem findings will then be presented by the pathologist in whose department the case was autopsied. Moderators and conference personnel will then answer questions that may arises as time permits. The clinical protocols of the cases to be presented will appear in a separate booklet to be sent with the formal program, so that members may have the opportunity of making their own diagnoses before the formal conferences.

Applications for tickets to Clinical-Pathological Conferences, unless otherwise indicated in the final program, may be made in advance by members on a regular application form which will accompany the program. Tickets will also be available at the Registration Bureau, Conrad Hilton Hotel. Non-members may not register by mail, but should secure their tickets directly at the meeting.

CP-1 Grand Ballroom, Conrad Hilton Hotel 4:00 P.M. to 5:00 P.M. Tuesday, April 6, 1954	CP-2 Boulevard Room, Conrad Hilton Hotel 4:00 P.M. to 5:00 P.M. Wednesday, April 7, 1954	CP-3 Grand Ballroom, Conrad Hilton Hotel 4:00 P.M. to 5:00 P.M. Thursday, April 8, 1954	CP-4 Boulevard Room, Conrad Hilton Hotel 3:00 P.M. to 4:00 P.M. Friday, April 9, 1954
	Case I		**Case I**
Moderator *George F. Strong Vancouver, B.C.	Moderator *Wallace M. Yater Washington	Moderator *Walter L. Palmer Chicago	Moderator **Maurice C. Pincoffs Baltimore
*Lennox G. Bell Winnipeg *Ray F. Farquharson Toronto *Edward S. Mills Montreal	*Ovid O. Meyer Madison *Hans Reese Madison *Wesley W. Spink Minneapolis	*Franklin M. Hanger New York *Hugh J. Morgan Nashville *Francis D. Murphy Milwaukee John R. Neefe Philadelphia Robert M. Zollinger Columbus	*Henry L. Bockus Philadelphia *Gordon B. Myers Detroit *Cyrus C. Sturgis Ann Arbor
Pathologist William Boyd Vancouver, B.C.	Pathologist *Samuel A. Levinson Chicago	Pathologist *Edwin F. Hirsch Chicago	Pathologist *Hans Popper Chicago
	Case II		**Case II**
	Moderator *Edward L. Bortz Philadelphia		Moderator *Marion A. Blankenhorn Cincinnati
	*William B. Bean Iowa City **William S. Middleton Madison William H. Riser Birmingham		*Thomas Findley New Orleans *Johnson McGuire Cincinnati *Randall G. Sprague Rochester
	Pathologist *Israel Davidsohn Chicago		Pathologist *Edwin F. Hirsch Chicago

* F.A.C.P.
** M.A.C.P.

THE CLINIC SESSIONS

Color Television of Medical Clinics

The following series of clinics will be televised in color daily, Tuesday through Friday, between 9:00 A.M. and 12:30 P.M., from St. Luke's Hospital to the television room on the Exhibition Floor of the Conrad Hilton Hotel.

Various institutions and their respective staffs are co-operating. Due to changing programs from one clinic to another, a slight lag will occur. However, it is believed that the times indicated will be approximately correct. This program is made possible through the co-operation of the Smith, Kline and French Laboratories, of Philadelphia. This year large screens will be used instead of the multiple small screens as formerly.

Admission by regular badge; no special tickets required.

Tuesday, April 6, 1954

9:00– 9:20 **Present Concept of a Liver Profile.**
MURRAY FRANKLIN, F.A.C.P., Associate Professor of Medicine, University of Illinois College of Medicine.

9:20– 9:40 **Acute Hepatitis.**
RICHARD B. CAPPS, F.A.C.P., Assistant Professor of Medicine, Northwestern University Medical School.

9:40–10:00 **Technique of Liver Biopsy.**
PHILIP JONES, M.D. (by invitation), Chicago.

10:00–10:20 **Pathology of Liver Disease.**
HANS POPPER, F.A.C.P., Associate Professor of Pathology, Northwestern University Medical School; Director, Department of Pathology, Cook County Hospital.

10:20–11:00 INTERMISSION.

11:00–11:20 **Examination of the Back.**
FRED SHAPIRO, M.D. (by invitation), Clinical Assistant Professor of Orthopedic Surgery, University of Illinois College of Medicine.

11:20–11:40 **How Insulin Acts.**
RACHMIEL LEVINE, M.D. (by invitation), Chicago.

11:40–12:00 **Dermatological Problems in Internal Medicine.**
THEODORE CORNBLEET, M.D. (by invitation), Clinical Professor of Dermatology, University of Illinois College of Medicine.

12:00–12:20 **Skin Testing of Some Common Skin Diseases.**
CLAYTON G. LOOSLI, M.D. (by invitation), Professor of Preventive Medicine, University of Chicago School of Medicine.

Wednesday, April 7, 1954

9:00– 9:20 **Early Signs of Multiple Sclerosis.**
BEN W. LICHTENSTEIN, M.D. (by invitation), Clinical Professor of Neurology, University of Illinois College of Medicine.

9:20– 9:40 **Shoulder-Hand Syndrome.**
DONALD S. MILLER, M.D. (by invitation), Professor and Chairman of Orthopedic and Traumatic Surgery, Chicago Medical School.

9:40–10:00 **Nutritional Neuropathies.**
HAROLD M. MANFREDI, M.D. (by invitation), Chicago.

10:00–10:20 **Elusive Brain Tumors.**
OSCAR SUGAR, M.D. (by invitation), Assistant Professor of Neurological Surgery, University of Illinois College of Medicine.

10:20–11:00 INTERMISSION.

11:00–11:20 **Clinical and Laboratory Problems in Viral Disease.**
ALBERT MILZER, M.D. (by invitation), Chicago.

11:20–11:40 **Antimicrobial Therapy in Tuberculosis.**
ROBERT H. EBERT, F.A.C.P., Associate Professor of Medicine, University of Chicago School of Medicine.

11:40–12:00 **Important Signs in the Diagnosis of Poliomyelitis.**
ARCHIBALD L. HOYNE, F.A.C.P., Emeritus Clinical Professor of Pediatrics, University of Chicago School of Medicine and University of Illinois College of Medicine; Professor of Pediatrics, Chicago Medical School.

12:00–12:20 **Diagnosis of Peripheral Vascular Disease.**
DAVID I. ABRAMSON, F.A.C.P., Clinical Assistant Professor of Medicine, University of Illinois College of Medicine.

Thursday, April 8, 1954

9:00– 9:20 **Cardiodynamics—Model Demonstrations.**
SIMON RODBARD, M.D. (by invitation), Chicago.

9:20– 9:40 **Diagnostic Techniques in the Evaluation of Patients for Cardiac Surgery.**
BENJAMIN M. GASUL, F.A.C.P., Associate Professor of Pediatrics, University of Illinois College of Medicine; Medical Director, Pediatric Cardiology, Cook County Hospital; and WILLIS J. POTTS, M.D. (by invitation), Associate Professor of Surgery, Northwestern University Medical School; Chairman, Department of Surgery, Children's Memorial Hospital.

9:40–10:20 **Arteriography.**
RICHARD E. BUENGER, M.D. (by invitation), Chicago.

10:20–11:00 INTERMISSION.

11:00–12:30 **Pulmonary Function Studies in Chest Diseases.**
DAVID B. RADNER, M.D. (by invitation), Director of Chest Department, Michael Reese Hospital; GEORGE A. SAXTON, M.D. (by invitation), Associate Professor of Medicine and Director of the Respiratory Center, Research and Educational Hospital, University of Illinois College of Medicine; RICHARD V. EBERT, F.A.C.P., Professor of Medicine, Northwestern University Medical School; and ALBERT H. ANDREWS, M.D. (by invitation), Professor of Bronchoesophagology, University of Illinois College of Medicine; Chief of Bronchoesophagology, Illinois Eye and Ear Infirmary.

Friday, April 9, 1954

9:00–10:20 **Psychosomatic Techniques for the Internist.**
FRANZ G. ALEXANDER, M.D. (by invitation), Clinical Professor of Psychiatry, University of Illinois College of Medicine; Director of Chicago Institute for Psychoanalysis; ROY R. GRINKER, M.D. (by invitation), Director, Institute for Psychosomatic and Psychiatric Research and Training, Michael Reese Hospital; and ALFRED P. SOLOMON, M.D. (by invitation), Clinical Associate Professor of Psychiatry, University of Illinois College of Medicine.

10:20–11:00 INTERMISSION.

11:00–12:20 **Chicago—A Medical Center in Radiation Therapy.**

IRWIN F. HUMMON, M.D. (by invitation), Associate Professor of Physical Medicine, Stritch School of Medicine of Loyola University; Therapeutic Radiologist, Cook County Hospital; ERICH UHLMANN, M.D. (by invitation), Director of Tumor Clinic, Michael Reese Hospital; and ROGER A. HARVEY, M.D. (by invitation), Professor of Radiology and Head of the Department, University of Illinois College of Medicine.

THE CLINIC SESSIONS

Clinics at Hospitals

The regular Hospital Clinics will be conducted on Tuesday and Thursday from 9:00 A.M. to 12:30 P.M. **Admission to the Hospital Clinics will require special tickets,** which will be issued to MEMBERS in advance of the Session and to NON-MEMBERS directly at the Registration Bureau in the Conrad Hilton Hotel. Application forms for tickets for the Hospital Clinics and Panel Discussions will be sent to all members with the program.

The Committee on Clinics is committed to a program of clinics in the true sense of that term—patients will be shown and discussed. A wide range of medical topics important to the clinician is offered.

The Committee on Transportation recommends the use of taxicabs for reaching the Hospital Clinics, and will arrange for an adequate number of taxicabs to be available also for the return trip.

Members are requested not to attempt to split clinics with one another, or with Panel Discussions. Tickets will be required for each and every one of the Hospital Clinics, unless specifically otherwise mentioned. The co-operation of every one in securing his clinic tickets will assist greatly in distributing the attendance according to the capacity of each meeting room. It is self-evident that a clinic arranged for fifty will lose its value for all if a hundred crowd in. Ticket registration, naturally, is the only effective method of keeping the attendance within the capacities indicated.

Member registration blanks for the clinics should be filled out and returned to the Executive Secretary promptly. Upon receipt at the College Office, proper tickets will be selected and held at the Registration Bureau in the Conrad Hilton Hotel, or, on the request of the member, will be mailed to him. Reservations by mail cannot be made after March 16, but reservations may be made in person at the Registration Bureau on the afternoon preceding any clinic day, provided tickets are still available.

Members who reserve clinic tickets are urgently requested to notify the Executive Secretary, and to return their tickets, if they find they will be unable to attend.

PROGRAM OF HOSPITAL CLINICS

Tuesday, April 6, 1954

A ALBERT MERRITT BILLINGS HOSPITAL

University of Chicago Clinics

(950 East 59th Street)

Room P-117, Pathology Auditorium

(Capacity, 260)

Presiding: Lowell T. Coggeshall

9:00– 9:30 Iron Deficiency Anemia.
Wm. F. Bethard.

9:30–10:00 Leukemia.
Leon O. Jacobson.

10:00–10:40 Idiopathic Thrombocytopenic Purpura.
Carl V. Moore, St. Louis, Mo.

10:40–11:00 Question and Answer Period on Hematology.

11:00–11:20 INTERMISSION.

11:20–12:00 Combinations of Drugs in the Treatment of Hypertension.
Robert W. Wilkins, Boston, Mass.

12:00–12:30 Sarcoidosis.
Robert H. Ebert.

B COOK COUNTY HOSPITAL CLINICS

(1835 West Harrison Street)

Medical Amphitheater, 8th Floor, Main Hospital

(Capacity, 111)

Presiding: Herman F. DeFeo

9:00–10:00 Massive Hemorrhage from Upper Gastro-intestinal Tract:
Differential Diagnosis.
Samuel Hyman.
Diagnostic Procedures.
Meyer J. Steinberg.
Prognosis.
Arthur Bernstein.
Treatment.
Edmund F. Foley.

Presiding: Melvin L. Afremow

10:00–11:00 Symposium on Liver Diseases:
Chronic Hepatitis.
Albert M. Snell, Palo Alto, Calif.
Diagnostic Aids, including Liver Biopsy.
Murray Franklin.
Liver Granulomata.
Gertrude M. Engbring.
Therapeutic Procedures.
Frederick Steigmann.

11:00–11:15 INTERMISSION.

11:15–12:30 Clinical-Pathological Conference:
Clinical Discussion.
S. Howard Armstrong, Jr., Isadore Pilot, George C. Turnbull and Abraham Rimmerman.
Pathologic Presentation.
Hans Popper.

12:30 Cook County Hospital Alumni Luncheon (Dining Room of the Karl A. Meyer Hall—Clinic visitors will be guests of the Alumni).

C EVANSTON HOSPITAL

Blackstone Hotel

(Michigan Avenue and East Balbo Drive)

Green Room

(Capacity, 75)

Presiding: Lowell D. Snorf

9:15– 9:20 Introduction.

9:20– 9:40 The Clinical Significance of Recent Observations in Atherosclerosis.
Arnold L. Wagner.

9:40–10:00 The Problem of Electrocardiographic Diagnosis of Myocardial Infarction in the Presence of Disturbed Ventricular Conduction.
Ernest G. McEwen.

10:00–10:20 Observations of Some Renal Diseases in Adults.
Maurice H. Wald.

10:20–10:30 INTERMISSION.

10:30–11:10 Chronic Ulcerative Colitis.
J. Arnold Bargen, Rochester, Minn.

11:10–11:30 Chronic Ulcerative Colitis, Color Proctoscopy.
Jerrold P. Nesselrod and Jay McK. Garner.

11:30–11:50 Substernal Pain due to Cervical Discopathy.
Samuel J. Lang.

11:50–12:15 The Open Airway in Poliomyelitis.
Martin H. Seifert.

D MERCY HOSPITAL—LOYOLA UNIVERSITY

(2537 South Prairie Avenue)

John B. Murphy Auditorium

(Capacity, 399)

Presiding: George F. O'Brien

9:00– 9:30 Problems in Diagnosis of Congenital Heart Disease.
Robert F. Dillon.

9:30–10:00 Electrolyte Problems.
Peter J. Talso.

10:00–10:45 Hypersplenism.
Charles E. Rath, Washington, D. C.

10:45–11:00 INTERMISSION.
11:00–11:45 Chronic Hepatitis.
Harold J. Jeghers, Washington, D. C.
11:45–12:15 Modern Concepts of Treatment of Tuberculosis.
William Lees.

E

MICHAEL REESE HOSPITAL

(East 29th Street and South Ellis Avenue)

Rothschild Auditorium

(Capacity, 240)

Presiding: Rachmiel Levine

9:00– 9:30 Intercapillary Glomerulosclerosis.
Robert C. Levy.
9:30–10:00 Collagen Diseases.
Matthew Taubenhaus.
10:00–10:30 Commissurotomy; Medical and Surgical Aspects.
Saul A. Mackler and Richard Langendorf.
10:30–11:00 REFRESHMENTS.
11:00–11:40 Diagnostic Cardiac Clinic.
William A. Brams and Jacob S. Golden.
11:40–12:00 Treatment of Uremia.
Richard Sternheimer.
12:00–12:30 Hemolytic Anemias.
Karl Singer.

F

MOUNT SINAI HOSPITAL

(2750 West 15th Place)

Kling Auditorium

(Capacity, 300)

Presiding: Martin M. Kirshen

9:00– 9:30 Medical Catastrophies.
Leonard Cardon.
9:30–10:00 Neurological Emergencies.
Ben W. Lichtenstein.
10:00–11:00 Hematology Clinic: Auto-Immune Hemolytic Anemias.
Charles A. Doan, Columbus, Ohio, Israel Davidsohn and Irving A. Friedman.
11:00–11:30 INTERMISSION.
11:30–12:00 Problems in Diagnosis of Chronic Diarrhea.
Erwin M. Kammerling, Armand Littman and Frederick Steigmann.
12:00–12:15 Demonstration of the Use of Alcohol-Oxygen Vapor in the Treatment of Paroxysmal Pulmonary Edema.
Aldo A. Luisada and Ruth Weyl.
12:15–12:30 Experimental Transplantation of Heart. The Behavior of the Transplanted Heart.
Aldo A. Luisada and Emanuel Marcus.

G PASSAVANT MEMORIAL HOSPITAL

(303 East Superior Street)

Nurses Lecture Room

(Capacity, 75)

Presiding: Richard H. Young

9:00– 9:20 Current Therapy of Acute and Chronic Leukemia.
Howard L. Alt.

9:20– 9:50 Diagnostic Approach in Patients with Anemia.
Frank H. Bethell, Ann Arbor, Mich.

9:50–10:10 Certain Aspects of Nephritis.
Edith B. Farnsworth.

10:10–10:30 Physiological Concepts in the Management of Severe Hypertension.
Howard A. Lindberg and Loyal Davis.

10:30–11:00 INTERMISSION.

11:00–12:30 Modern Concepts of Peptic Ulcer.
Panel:
Clifford J. Barborka, Chairman; Walter W. Carroll, Edmund A. Gorvett, R. Burns Lewis and E. Clinton Texter, Jr.

H PRESBYTERIAN HOSPITAL

Senn Hall, North Amphitheater

(1748 West Harrison Street)

(Capacity, 125)

Presiding: Alva A. Knight

9:00– 9:10 Introductory Remarks.
Ernest E. Irons.

9:10– 9:40 Some Aspects of the Problem of Obesity.
Maurice C. Pincoffs, Baltimore, Md.

9:40– 9:55 Rheumatoid Spondylitis.
Evan M. Barton.

9:55–10:10 Non-Allergic Asthma.
George W. Stupfy.

10:10–10:30 Certain Features of Adrenalectomy in Metastatic Carcinoma.
Samuel G. Taylor, III, James H. McDonald and Harry W. Southwick.

10:30–11:00 INTERMISSION.

ULCERATIVE COLITIS

11:00–11:15 Medical Management—Methods and Results.
Osmund H. Akre.

11:15–11:30 Electrolyte Studies.
Douglas A. MacFadyen.

11:30–11:45 Nutritional Studies.
Robert M. Kark.

11:45–12:00 Evaluation of Surgical Treatment.
R. K. Gilchrist.

12:00–12:15 Pathology.
George M. Hass.

12:15–12:30 Discussion.
Herbert C. Breuhaus.

9:00–12:30 Demonstration—Vector Electrocardiography.
John S. Graettinger.
(Available to those who attend the Clinic, if interested.)

J **ST. LUKE'S HOSPITAL**

(1439 South Michigan Avenue)

Ryerson Lounge, Schweppe Nurses Residence

(Capacity, 125)

Presiding: Grant H. Laing

9:00– 9:30 Twenty Years' Observation on the Course of Elevated Blood Pressure in 500 Women between 70 and 100 Years of Age.
Howard Wakefield.

9:30–10:00 Evaluation and Management of the Hypertensive Patient.
Eugene B. Ferris, Atlanta, Ga.

10:00–10:45 The Surgical Treatment of Hypertension.
Geza de Takats.

10:45–11:00 INTERMISSION.

11:00–11:25 Ureteral Tumors as a Cause of Bizarre Abdominal Symptoms—Illustrated with a Series of Case Studies.
William J. Baker and Edwin C. Graf.

11:25–11:55 Demonstration of Patients Five Years Following Pneumonectomy.
Willard Van Hazel and Robert J. Jensik.

11:55–12:30 Morbidity and Death Preventable by Inhalation Therapy.
Albert H. Andrews.

K **UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE RESEARCH AND EDUCATIONAL HOSPITALS**

(1853 West Polk Street)

Meeting Room 106

(Capacity, 200)

Presiding: Norman B. Roberg

9:00– 9:25 Porphyria.
Robert M. Kark.

9:25– 9:50 Treatment of Bacterial Meningitis.
Mark H. Lepper.

9:50–10:15 Renal Changes (Biopsy) Associated with Chronic Bacturia, Including the Effects of Antibiotic Therapy.
George G. Jackson.

10:15–10:40 Treatment of Bacterial Endocarditis.
Harry F. Dowling.

10:40–11:00 INTERMISSION and COFFEE.

11:00–11:40 The Management of Congestive Heart Failure with Particular Emphasis on Hot and Humid Environments.
George E. Burch, New Orleans, La.

11:40–12:05 Cardiac Emergencies Arising Postoperatively.
Norman B. Roberg.

12:05–12:30 Ill Results after Mitral Commissurotomy.
Ford K. Hick.

L VETERANS ADMINISTRATION RESEARCH HOSPITAL

(In affiliation with Northwestern University Medical School)

(333 East Huron Street)

Auditorium

Presiding: Thomas F. Barrett

9:00– 9:45 Congestive Heart Failure.
Eugene A. Stead, Jr., Durham, N. C.

9:45–10:30 Cor Pulmonale.
Richard V. Ebert.

10:30–11:00 INTERMISSION.

11:00–11:45 Mitral Stenosis.
Craig W. Borden.

11:45–12:30 Coronary Thrombosis.
Robert P. Gilbert.

M VETERANS ADMINISTRATION HOSPITAL HINES, ILL.

Auditorium

Veterans Administration Research Hospital

(333 East Huron Street)

Chicago

(See Thursday only)

N WESLEY MEMORIAL HOSPITAL

(250 East Superior Street)

Staff Room

(Capacity, 125)

Presiding: Gilbert H. Marquardt

9:00–10:00 Clinical-Pathological Conference.
William B. Bean, Iowa City, Iowa, and Thomas C. Laipply.

10:00–10:40 Lesions of the Colon.
Arthur E. Mahle and A. H. C. Cannon.

10:40–10:50 COFFEE.

10:50–11:25 Treatment of Collagen Diseases with Steroid Hormones.
David E. Markson.

11:25–12:00 Treatment of Edema.
George M. Cummins, Jr., and Gilbert H. Marquardt.

Thursday, April 8, 1954

A **ALBERT MERRITT BILLINGS HOSPITAL**

University of Chicago Clinics

(950 East 59th Street)

Room P-117, Pathology Auditorium

(Capacity, 260)

Presiding: Walter L. Palmer

9:00– 9:30 Treatment of Rheumatoid Arthritis.
Delbert M. Bergenstal.

9:30–10:00 Problems in the Treatment of Diabetes.
Henry T. Ricketts.

10:00–10:30 The Current Status of Gastric Antisecretory Drugs.
Joseph B. Kirsner.

10:30–10:45 INTERMISSION.

10:45–11:15 The Rôle of ACTH and Cortisone in the Treatment of Ulcerative Colitis.
Walter L. Palmer.

11:15–12:00 Pancreatitis.
Mandred W. Comfort, Rochester, Minn.

12:00–12:30 Question and Answer Period on Gastro-enterology.

B **COOK COUNTY HOSPITAL CLINICS**

(1835 West Harrison Street)

Medical Amphitheater, 8th Floor, Main Hospital

(Capacity, 111)

Presiding: Francis L. Foran

9:00–10:00 Symposium on Heart Disease Amenable to Surgery:
Congenital Heart Disease.
Benjamin M. Gasul.
Pericarditis.
Don C. Sutton.
Valvular Disease.
Louis Feldman.
Surgery Aspects.
Egbert H. Fell.

Presiding: Eugene F. Traut

10:00–11:15 Hematology Clinic:
Presentation of Hematologic Case Problems.
Steven O. Schwartz, Irving A. Friedman and Robert K. Nixon.
Discussant.
Cyrus C. Sturgis, Ann Arbor, Mich.

11:15–11:30 INTERMISSION.

Presiding: Jacob W. Fischer

11:30–12:30 Chronic Pulmonary (non-Tuberculosis) Disease:
Differential Diagnosis.
George C. Turner.
Diagnostic Procedures.
Louis C. Morris.
Medical Treatment.
Earl A. Zaus.
Surgical Treatment.
George W. Holmes.

C EVANSTON HOSPITAL

Blackstone Hotel

(Michigan Avenue and East Balbo Drive)

Green Room

(Capacity, 75)

Presiding: Richard H. Young

9:15– 9:20 Introduction.

9:20– 9:40 Pitfalls in the Diagnosis of Vascular Accidents.
Joseph A. Tarkington.

9:40–10:00 Unusual Problems in the Management of Heart.
Franklin A. Kyser.

10:00–10:20 Juvenile Rheumatoid Arthritis.
Gordon W. Raleigh and Herbert R. Kobes.

10:20–10:30 INTERMISSION.

10:30–11:10 (*Title to be announced.*)
Charles A. Doan, Columbus, Ohio.

11:10–11:30 Complications of Pancreatitis.
Lowell D. Snorf.

11:30–11:50 Decreased Insulin Tolerance following Myocardial Infarction.
Leonard F. Jourdonais.

11:50–12:15 Perforating Peptic Esophagitis.
John M. Dorsey.

D MERCY HOSPITAL—LOYOLA UNIVERSITY

(2537 South Prairie Avenue)

John B. Murphy Auditorium

(See Tuesday only)

E MICHAEL REESE HOSPITAL

(East 29th Street and South Ellis Avenue)

Rothschild Auditorium

(Capacity, 240)

Presiding: Jacob Meyer

9:00– 9:20 Diagnostic Clinic in Peripheral Vascular Diseases.
David I. Abramson.

9:20– 9:40 Medical Aspects of Peptic Ulcer.
David H. Rosenberg.

9:40–10:10 Psychosomatic Aspects of Peptic Ulcer.
Roy R. Grinker.

10:10–10:40 Granulomatous and Inflammatory Diseases of Liver. Diagnostic and Therapeutic Problems.
Mitchell A. Spellberg.

10:40–11:00 REFRESHMENTS.

11:00–12:30 Clinical-Pathological Conference.
Otto Saphir, and Burrill B. Crohn, New York, N. Y.

F MOUNT SINAI HOSPITAL

(2750 West 15th Place)

Kling Auditorium

(Capacity, 300)

Presiding: Ellis B. Freilich

9:00– 9:45 Chest Clinic: Experiences with Psittacotic Pneumonia.
David B. Radner.

9:45–10:00 Palliative Esophagoplasty for Esophageal Obstruction.
Saul A. Mackler.

10:00–11:00 Iatrogenic Electrolyte Disturbances.
Peter Gaberman, Harry F. Weisberg and Herman L. Eisenberg.

11:00–11:30 INTERMISSION.

11:30–12:00 The Use of Radioactive Isotopes in Treatment of Congestive Failure.
Donald H. Atlas, Ervin Kaplan and Richard H. Kosterlitz.

12:00–12:30 Practical Procedures in Bedside Diagnosis of Peripheral Vascular Diseases.
David I. Abramson.

G PASSAVANT MEMORIAL HOSPITAL

(303 East Superior Street)

Nurses Lecture Room

(Capacity, 75)

Presiding: Laurence E. Hines

9:00– 9:20 The Management of Severe Asthma.
Samuel M. Feinberg.

9:20– 9:40 Selective Treatment of Diabetes Mellitus.
Arthur R. Colwell, Sr.

9:40–10:10 Hyperfunctioning Lesions of the Adrenal Cortex.
Randall G. Sprague, Rochester, Minn.

10:10–10:30 Blood "Corticoid" Concentration in Health and Disease.
Smith Freeman.

10:30–11:00 INTERMISSION.

11:00–12:30 Clinical-Pathological Conference on Coronary Pathology.
Chauncey C. Maher, William B. Wartman, Frederick W. Fitz, Theodore R. Van Dellen, John A. Mart and Hugh A. Flack.

H PRESBYTERIAN HOSPITAL

(1753 West Congress Street)

(See Tuesday only)

J ST. LUKE'S HOSPITAL

(1439 South Michigan Avenue)

Ryerson Lounge, Schweppe Nurses Residence

(Capacity, 125)

Presiding: Richard B. Capps

9:00– 9:10 Introductory Remarks.

9:10– 9:30 The Prognosis in Cirrhosis of the Liver.
Albert M. Snell, Palo Alto, Calif.

9:30– 9:50 The Rôle of Hemolysis in the Production of Jaundice and Anemia in Cirrhosis.
George V. LeRoy.

9:50–10:10 Chronic Cholangiolitic Hepatitis and Partial Common Duct Obstruction.
Philip N. Jones.

10:10–10:30 INTERMISSION.

10:30–10:50 The Demonstration of Esophageal Varices by Esophagoscopy.
Paul H. Holinger.

10:50–11:20 The Surgical Approach to the Problem of Varices.
Ormand C. Julian.

11:20–11:50 Medical Aspects of Shunt Surgery.
Victor M. Sborov, San Francisco, Calif.

K UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE RESEARCH AND EDUCATIONAL HOSPITALS

(1853 West Polk Street)

Meeting Room 106

(Capacity, 200)

Presiding: Max M. Montgomery

9:00– 9:25 Sheehan's Syndrome.
Murray Franklin.

9:25– 9:50 Mechanical Aids to Breathing in Diseases of the Lung.
George A. Saxton.

9:50–10:15 Cirrhosis of the Liver.
Hyman J. Zimmerman.

10:15–10:40 Epilepsy—Use of Drugs.
Frederick W. Stamps.

10:40–11:00 INTERMISSION and COFFEE.

11:00–11:30 Multiple Myeloma.
LeRoy H. Sloan and Louis R. Limarzi.

11:30–11:55 Diffuse Collagen Disease.
S. Howard Armstrong, Jr.

11:55–12:15 Management and Rehabilitation of Patients with Intrinsic Bronchial Asthma.
Max Samter.

12:15–12:30 Gouty Arthritis.
Max M. Montgomery.

L VETERANS ADMINISTRATION RESEARCH HOSPITAL

(In affiliation with Northwestern University Medical School)

(333 East Huron Street)

(See Tuesday only)

M VETERANS ADMINISTRATION HOSPITAL HINES, ILL.

Auditorium

Veterans Administration Research Hospital

(333 East Huron Street)

Chicago

Presiding: Lyle A. Baker

9:00– 9:30 Keratoderma Blenorrhagica.
Max M. Montgomery.

9:30–10:00 Association of Boeck's Sarcoid and Polyarteritis Nodosa.
S. Howard Armstrong, Jr.

10:00–10:30 Disseminated Coccidioidomycosis and Blastomycosis.
Isadore Snapper.
10:30–11:00 INTERMISSION.
11:00–11:30 Hemochromatosis—Discussion of Iron Metabolism.
Martin Kleckner.
11:30–12:00 Xanthomatous Biliary Cirrhosis.
Robert M. Kark.

N

WESLEY MEMORIAL HOSPITAL

(250 East Superior Street)

Staff Room

(Capacity, 125)

Presiding: Paul S. Rhoads

9:00– 9:40 Clinic—Acute and Chronic Leukemia.
Ovid O. Meyer, Madison, Wis.
9:40–10:20 Hypersplenic Syndrome.
Henry Wilson.
10:20–10:30 COFFEE.
10:30–11:00 Treatment of Nephrotic Syndrome with Nitrogen Mustard.
Frederic A. Lestina and Smith Freeman.
11:00–11:30 Operated Intro-atrial Septal Defects.
Walter S. Priest.
11:30–12:00 Congenital Heart Disease in Adults.
Gerald H. Graham.

SEMINARS IN MEDICINE OF MEXICO

(Following the 35th Annual Session, Chicago, April 5–9, 1954)

Through the generous coöperation of Dr. Ignacio Chávez, F.A.C.P., Governor of the American College of Physicians for Mexico, and Dr. Salvador Zubirán, F.A.C.P., of Mexico, the following scientific program has been arranged in connection with a post-convention tour immediately following the 35th Annual Session of the College in Chicago. Dr. Chávez is Professor of Medicine at the National University School of Medicine of Mexico, is the Director of the famous Instituto de Cardiología of Mexico, and has most successfully organized and directed postgraduate courses in cardiology for the A.C.P. Dr. Zubirán is Director of the widely recognized Hospital de Enfermedades de la Nutricion and has been a distinguished Fellow of the A.C.P. for many years. Together they have obtained the coöperation of several representative institutions, such as, in addition to their own, the Hospital General, Hospital Infantil, Instituto de Enfermedades Tropicales, et al, and the participation on the program of many distinguished Mexican medical authorities.

The Seminar party, limited to 100, will leave Chicago at about 10:30 A.M., April 10, by DC-6 Flagships of the American Airlines, arriving in Mexico City that same evening. They will be quartered at the Hotel Geneve. A get-together dinner will be held that evening.

Program—Sunday, April 11

Morning motor trip to the Floating Gardens, Xochomilco. Afternoon will be free to visit a bullfight if desired (admission is not included in price of trip).

Program—Monday, April 12

Scientific Session at the Instituto Nacional de Cardiología

A.M.

8:30 **Inspection of the Instituto Nacional de Cardiología.**

9:30 **The X-Ray Diagnosis of Pulmonary Agenesia.**
DR. N. DORBECKER.

10:10 **Electrocardiogram of Acute Cor Pulmonale.**
DR. D. SODI PALLARES.

10:30 **Hemodynamic Studies of Atrial Septal Defect.**
DR. R. LIMÓN.

11:00 **Questions and Answers.**

11:10 **Recess—Refreshments.**

11:25 **A New Sign of Myocardial Infarction in Case of Left Bundle Branch Block.**
DR. E. CABRERA.

11:55 **Clinical Findings in Pulmonary Infarction.**
DR. I. CHÁVEZ.

12:25 **Cardiac Involvement in Collagen Diseases.**
DR. J. ROBLES GIL.

12:55 **Questions and Answers.**

1:10–2:30 **Luncheon.**

By the Instituto Nacional de Cardiología in its physicians' dining room, for the physicians in attendance and for the professors in charge of delivering the lectures.

P.M. **Sightseeing tour around the City's business and residential sections.**

Visit the National Palace to see the Calendar Stone, the former home of Emperor Maximilian in fashionable Chapultepec Park, and the Church of Guadalupe, the most sacred shine in the Republic.

While the scientific program is in session in the morning, the ladies will have an opportunity to visit the fascinating shops—hand made fabrics, table covers, silver articles; they will lunch at the hotel.

Program—Tuesday, April 13

Scientific Session at the Hospital de Enfermedades de la Nutricion

A.M.

8:30 **Inspection of the Hospital de Enfermedades de la Nutricion.**

9:30 **(1) Introduction.**
Dr. S. Zubirán.

(2) Intestinal Amoebiasis.
Drs. E. J. Becerra, R. Hernandez de la Portilla and E. Rojas.

(3) Hepatic Amoebiasis.
Drs. B. Sepúlveda and F. Bassols.

(4) Questions and Answers.

10:50 **Recess.**

11:00 **(1) Types and Incidence of Anemias in Malnutrition.**
Dr. J. Báez Villaseñor.

(2) Therapeutic Approach to These Anemias.
Dr. L. Sánchez Medal.

(3) Questions and Answers.

11:50 **Recess—Refreshments.**

12:00 **Systemic and Local Effects of the Administration of Steroids in Patients with Cancer of the Cervix.**
Drs. G. Montaño and F. Gómez Mont.

1:00 **Adjournment.**

P.M. **A Motor trip to Teotihuacan, the Home of the Gods, for lunch.** Here will be seen the Pyramids of the Sun and Moon, the highest artificial mounds in North America, and the Temple of Quetzalcoatl.

Evening

8:30 Dinner at Ambassadeurs restaurant, given by the Mexican members of the American College of Physicians to Officials and their wives.

Program—Wednesday, April 14

Scientific Session at the Instituto Nacional de Cardiología

A.M.

9:00 **Treatment of Third Degree Malnutrition without Commercial Vitamins.**
Dr. F. Gómez.

Questions and Answers.

9:40 **Peptic Esophagitis.**
DR. A. AYALA GONZÁLEZ.
Questions and Answers.

10:20 **Thomography in the Diagnosis of Pulmonary Diseases.**
DR. D. ALARCÓN.
Questions and Answers.

11:00 **Recess—Refreshments.**

11:15 **Economic and Social Factors in the Etiology of the So-called Tropical Diseases.**
DR. M. MARTÍNEZ BÁEZ.
Questions and Answers.

11:50 **Comparative Value of Animal Protein and Vegetable Protein in Human Nutrition.**
DR. S. ZUBIRÁN.
Questions and Answers.

12:25 **Diagnosis of the Atypical Forms of Patent Ductus Arteriosus.**
DR. I. CHÁVEZ.
Questions and Answers.

Luncheon.
Served at the adjournment of the meeting at Dr. Zubirán's country house, located in the outskirts of Mexico City, San Jerónimo (Lidice), to the doctors and their wives.

P.M. An afternoon motor trip to the Desert of Lions, San Angel, Pedrigal and other suburban districts.

Program—Thursday and Friday, April 15–16

A two-day motor trip to Taxco, a village cradled by mountains and dominated by the cathedral, and Cuernavaca, a picturesque old city where the Aztec kings had their summer homes, where Cortez and Emperor Maximilian lived in the summer, and where official and diplomatic Mexico and others of wealth and fashion now have their residences.

Program—Saturday, April 17

An all day motor tour by a mountain road of great beauty passing the mighty snow-capped peaks of Ixtaccihuatl and Popocatepetl, lush green valleys, Indian villages and markets, Cholula with its Aztec pyramid, and reaching Puebla, the "Rome of Mexico," for lunch. Afternoon, a drive about the City to visit the homes and factories of the pottery, onyx and tile workers. The manufacture of ceramics is an ancient art in Mexico.

Evening
A Farewell Dinner.

Program—Sunday, April 18

Transfer to the Airport for departure as required, 7:30 A.M. or 10:30 A.M.

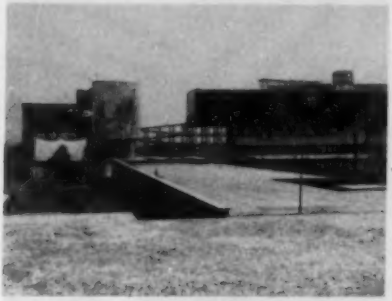
The Price: The Fiesta fare on which the tour was originally priced will have been discontinued in March. The Blue Ribbon Aircoach service of the American Airlines, which has proved popular, takes its place. However, the aircoach service

does not provide meals en route, but otherwise includes the same equipment and service. There are now two inclusive fares available from Chicago—regular first-class at $434.75 each, two in a room; Blue Ribbon Aircoach at $362.40 each, two in a room. The first is more, the latter less than the original quotation.

The Price Does Not Include: Four dinners in Mexico City for your convenience in sampling well-known restaurants; tips to drivers and tour guides, waiters and maids in Mexico City for your better service; beverages not on the regular menu; purchases, taxi transfers for shopping and Seminars, laundry, or other items of a personal nature.

Baggage Allowance: With Mexico City as destination it is 66 pounds. Dress will be informal. Travel light. Baggage will be heavier on the return because of purchases. $200 worth of purchases may be brought back duty free.

The Conductor in Charge will be Mr. Leon V. Arnold, 36 Washington Square West, New York 11, N. Y. A deposit of $50.00 will hold your place; if you find later you cannot go, your deposit will be refunded promptly. Mr. Arnold will be in charge of all travel arrangements, and all reservations should be made through him.



National University of Mexico View of Medical College



National University of Mexico Close-up of Medical College



National University of Mexico Library (without windows to provide more space for books and with artificial climate to conserve the books better).



National University of Mexico Administrative Center and Lecture Halls



National Institute of Cardiology



Hospital de Enfermedades de la Nutricion



House on a Hillside in Taxco, Mexico



Famous Aztec Calendar Used to Mark Time for the Aztec Indians More Than 500 Years Ago.



The Floating Gardens, Xochomilco



Chapultepec Palace, Mexico City



Borda Cathedral, Taxco

CHICAGO—HOST CITY TO THE NATION

Setting for the 35th Annual Session of the American College of Physicians, April 5–9, 1954

DURING the week of April 5, 1954, thousands of members of the College will convene in Chicago, and will have ample opportunity to discover why this city has earned the reputation of being the "Convention City of the World."

Some of the things which have led to this title are the following: Chicago is the second largest city in America, fourth largest in the world, with a metropolitan population of 5½ million. Yet only 100 years ago this city was an obscure Indian outpost!

It is the transportation hub of the continent, and 22 trunk railroads make it the world's railroad capital. More than 1700 trains arrive and depart daily, carrying almost 350,000 passengers. Chicago is the world's busiest air transportation center. Fifteen major airlines handle yearly over five million passengers. This is the heaviest volume of passenger traffic handled anywhere in the world.

A robust, youthful city, Chicago offers a variety of attractions for the visitor. It is a city of magnificent lake front beaches, beautifully landscaped parks and well-traveled boulevards. It is the home of great universities, fine art galleries, museums and libraries, and also, by way of contrast, of the world's largest stockyards. The "magnificent mile" on North Michigan Avenue houses some of the world's smartest shops catering to the expensive tastes of milady.

To say that Chicago is a city of commerce is an understatement, for it is an industrial colossus. The leading industries are meat packing, iron and steel, machinery, electrical apparatus, petroleum refining, paints and chemicals, printing and publishing, clothing, railroad car manufacturing, farm equipment, jewelry, toys, furniture, radio, television and electronic equipment, plastics, aircraft parts and building materials. And *this is only a partial list!*

A FEW MEDICAL LUMINARIES. . . .

This is not the time, nor is there space to recount a detailed medical history of Chicago. However, there are certain outstanding highlights worthy of mention, and there are a few great names without which no medical history of this city would be complete.*

The history of medicine in Chicago begins with the establishment of Fort Dearborn in August, 1803. Troops under Captain John Whistler arrived at the fort, after a 19 day march from Detroit, to build the fort. With them was a Dr. William C. Smith. From that time on, army surgeons were part of the regular garrison.

* The material used is adapted from an address by William Allen Pusey before the Institute of Medicine in January, 1940.

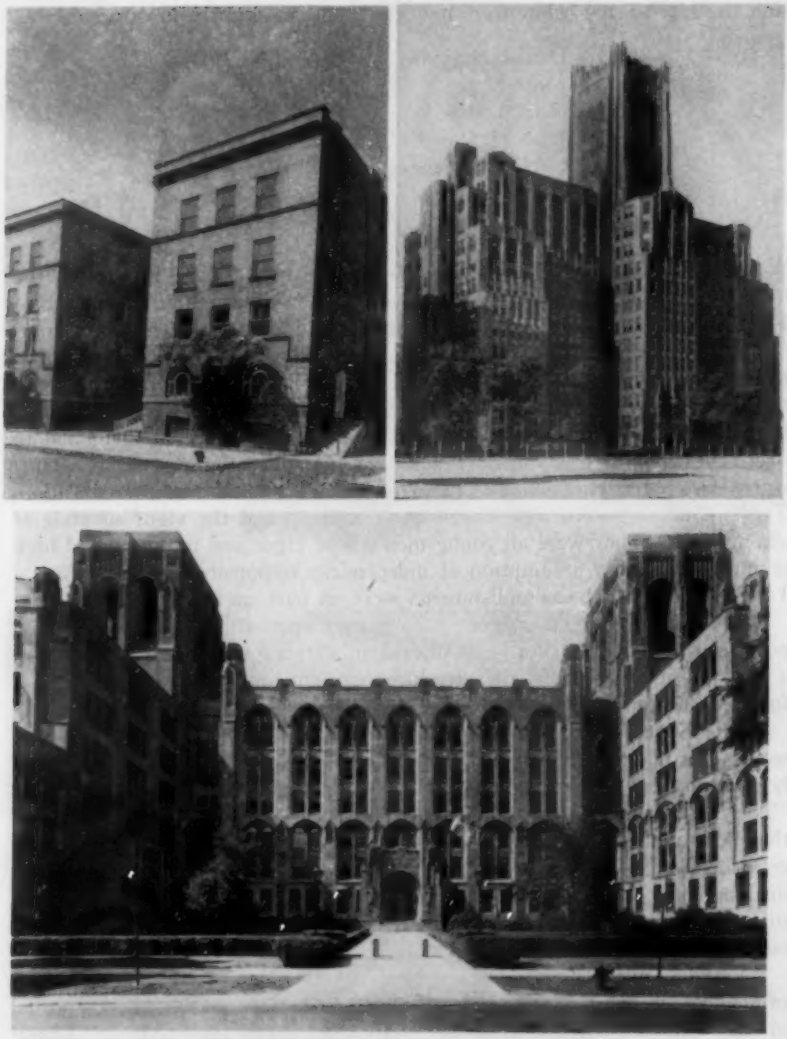


The Medical District on the city's near West side which makes Chicago one of the leading medical centers in the world. This 305-acre area contains the largest concentration of medical facilities in the United States, and has an evaluation of $150,000,000.

It presently has 11 professional schools, including the University of Illinois College of Medicine, Stritch School of Medicine of Loyola University, and Chicago Medical School, as well as the Cook County Graduate School of Medicine.

Hospital facilities include Cook County Hospital, the University of Illinois Research and Educational Hospitals, Presbyterian Hospital, the Veterans Administration Hospital, and the Chicago State Tuberculosis Sanitarium.

One out of every five physicians in the United States had some phase of his training or education in this Medical Center.



Upper left—Chicago Medical School
Upper right—Northwestern University Medical School
Bottom—Albert Merritt Billings Hospital and University of Chicago School of Medicine

While there have been many great men in the history of Chicago medicine, the seven listed below were unquestionably among the most notable:

Daniel Brainard	1812–1866
John Evans	1814–1897
N. S. Davis	1817–1904
John H. Rauch	1828–1894
Christian Fenger	1840–1902
Frank Billings	1854–1932
Ludvig Hektoen	1863–1951

Of these men Pusey says, ". . . the early lives of these men fit in the familiar pattern of success. They were all Americans by birth, except Fenger: they came of virile stock, of families of a class that have the comforts of life and believe in education and religion, the class of people that have been the builders of the past and are the hope for the future in these troubled democratic times. These men always had duties and responsibilities and got their higher education by effort, but none of them had to overcome crippling hardships. Fenger was a Dane of the same class. They were physicians who had general education and good medical education. They all wrote good English, and most of them had the vigorous style of strong men. They were all young men whose vigor and initiative had been stimulated by early assumption of independent responsibilities."

Their individual accomplishments were, in part, as follows:

Daniel Brainard—A surgeon who gained international reputation. He possessed the qualities of a great physician, a strong scientific bent, and was a first-rate investigator. He introduced experimental medicine in Chicago, founded and guided Rush Medical College.

John Evans—A Quaker whose first notable achievement was his pioneer work in providing efficient and humane care for the insane in Indiana. A hospital builder, he founded and edited the first medical journal in Chicago, "The Northwest Medical and Surgical Journal." An advocate of the belief that communicable diseases were contagious, he was responsible for the enactment of the national quarantine law. He built railroads, churches, distributed his large personal fortune among worthy charities. A statesman in every sense of the word, he founded Northwestern University, and later became the Governor of Colorado.

Nathan Smith Davis—The author of the standard text on the practice of medicine in his day. A great teacher and educator, he edited the Journal of the American Medical Association from its establishment in 1833 until 1889. He was particularly helpful in studying the problems of disease and sanitation as they affected the Chicago area.

John H. Rauch—As Executive Officer of the Illinois Department of Public Health, his services were outstanding. He was responsible for the creation of an efficient Board of Health, and did a great deal for improved

Stritch School of Medicine of Loyola University





University of Illinois College of Medicine

sanitation, the control of epidemics, the enforcement of quarantine laws. He also worked for rigid pure food and drug laws, and was largely responsible for the Chicago Park System.

Christian Fenger—A man of culture, extraordinary training and wide experience, his service to medicine in Chicago was his new concept of pathology, and his emphasis on the science of bacteriology as it related to antiseptic sugery.

Frank Billings—Not only a remarkable physician, but a great leader of men and champion of worthy causes. Billings was tremendously interested in education and in community improvement. His outstanding contribution was the building of the medical school at the University of Chicago.

Ludvig Hektoen—Chairman of the National Research Council, he was also consultant to the United States Public Health Service, where he directed research on cancer. He exerted a real and lasting influence on modern scientific medicine in America. A great teacher in pathology, he gathered about him a most distinguished group of investigators.

From the above it can be seen that Chicago has done a great deal to advance the cause of medical education, medical research, and medicine itself. It now has a concentration of facilities and medical talents which few other cities can offer, including numerous outstanding hospitals and five approved medical schools. Chicago is also the home of a dozen internationally known medical organizations, including the American Medical Association, the American College of Surgeons, the Association of American Medical Colleges, the American Hospital Association, and the Chicago Medical Society.

Today, the medical profession of Chicago, inspired by the heritage of its medical history, is continuing in this tradition so that the future of medicine in this great city may be even more noteworthy than has been its past.



Mercy Hospital



Michael Reese Hospital



Wesley Memorial Hospital



Passavant Memorial Hospital



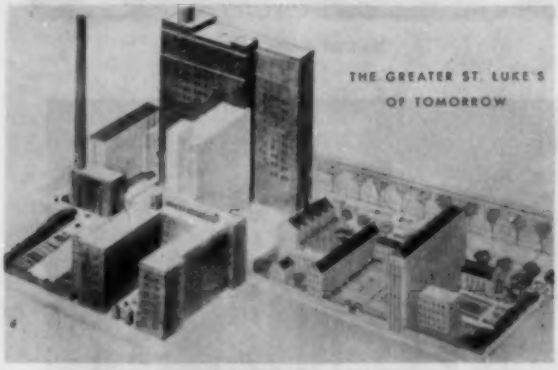
Evanston Hospital



Veterans Administration Hospital, Hines, Ill.



Mount Sinai Hospital



St. Luke's Hospital



Presbyterian Hospital



Wrigley Building at night



Oak Street Beach



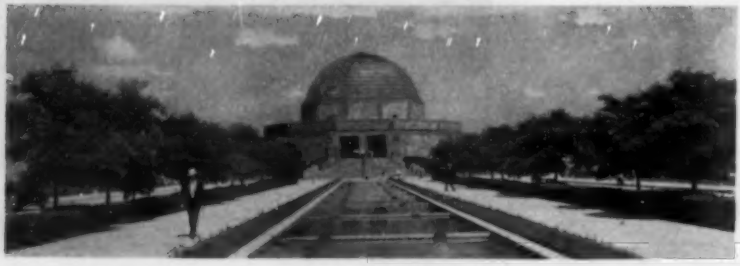
The Conrad Hilton Hotel, Convention Headquarters, and formerly The Stevens



The Merchandise Mart



Buckingham Fountain



The Adler Planetarium



Fig. 1 "Roentgen examination . . . revealed the ulcer to be very much in evidence."



Fig. 2 In ten weeks "the ulcer niche was no longer in evidence roentgenologically or gastroscopically."

Clinical Evaluation of Pro-Banthine®

The case report described below offers significant evidence of the high potency in low dosage of the new, well-tolerated anticholinergic agent, Pro-Banthine.

"M. D., female, aged 48, had a posterior gastrojejunostomy 14 years ago for duodenal ulcer. The patient was fairly well until nine months ago when severe, intractable pains occurred. She was hospitalized and a subtotal gastrectomy was done.

"She remained well for only a few months and was referred to us because of recurrence of very severe pain and marked weight loss. Roentgen study revealed a fairly large ulcer niche on the gastric side of the anastomosis.

"The patient had been on various types of antacids and sedatives without relief from pain. She was given 60 mg. of Pro-Banthine q.i.d. and within 72 hours was able to sleep through the night for the first time in weeks.

"At the end of two weeks of such treatment the patient had absolutely no pain and felt that she had been 'cured.' Roentgen examination at this time revealed the ulcer to be very much in evidence (*Fig. 1*). Much persuasion was necessary to make the patient realize the importance of maintaining her diet and therapy.

"Ten weeks of controlled regulation was necessary before we were satisfied that the ulcer niche was no longer in evidence roentgenologically or gastroscopically (*Fig. 2*).

"She has been maintained on 30 mg. [q. i. d.] of Pro-Banthine for almost five months with no recurrence of symptoms."[1]

Pro-Banthine (*brand of propantheline bromide*), the new, improved anticholinergic agent, is more potent and, consequently, a smaller dosage is required and side effects are greatly reduced or absent. It is available in 15 mg. tablets as well as in tablets (15 mg.) with Phenobarbital (15 mg.) and in 30 mg. ampuls.

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1. Schwartz, I. R.: Personal communication, Feb. 9, 1953.



PROTECTION you need a WHOLE RAINCOAT

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MEJALIN—and only MEJALIN—supplies all 11 identified B vitamins plus liver and iron

B complex protection may be needed by that overworked executive with "no time to eat" . . . by that balky youngster that turns up his nose at mealtime . . . by your elderly patient who doesn't like the right foods—in fact, by anyone who eats poorly or sporadically or who requires an extra measure of vitamin support.

Since "vitamins, especially those of the B complex, are closely interrelated" and "lack of availability of any one may affect the metabolism of the others,"[1] the importance of a complete B vitamin product is apparent.

Mejalin provides all the identified B vitamins plus liver and iron as an extra safeguard for good nutrition.

Two exceptionally pleasant dosage forms assure patient acceptance.

1. Therapeutic Nutrition, Publication 234, National Research Council, 1952.



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Thiamine	1 mg.
Riboflavin	1 mg.
Niacinamide	10 mg.
Pyridoxine hydrochloride	0.2 mg.
Pantothenic acid	1 mg.
Choline	50 mg.
Inositol	20 mg.
Vitamin B_{12} (crystalline)	3 mcg.
Folic acid	0.2 mg.
Biotin	0.02 mg.
Para-aminobenzoic acid	0.5 mg.
Liver fraction	300 mg.
Iron (from ferrous sulfate)	7.5 mg.

Mejalin Liquid contains panthenol and soluble liver fraction N. F.; Mejalin Capsules contain calcium pantothenate and desiccated liver N. F..

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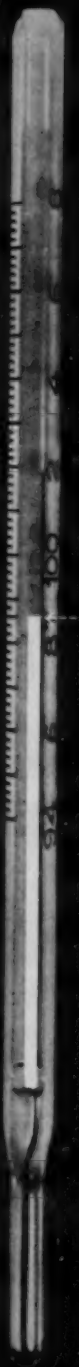
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J. B. Roerig and Company announces the availability of

a basic new anti-infective agent



pneumococcal infections,
including pneumonia,
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with or without bacteremia,
including follicular tonsillitis,
septic sore throat,
scarlet fever,
pharyngitis,
cellulitis;
urinary tract infections due to
susceptible organisms, and
meningitis;
many staphylococcal infections,
with or without bacteremia,
including furunculosis,
septicemia,
abscesses,
impetigo,
acute otitis media,
ophthalmic infections,
susceptible urinary tract infections,
bronchopulmonary infections,
acute bronchitis,
pharyngitis,
laryngotracheitis,
tracheobronchitis,
sinusitis,
tonsillitis,
otitis media, and
osteomyelitis;
certain mixed bacterial infections;
soft tissue infections due to
susceptible organisms.

BASIC

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BASIC chemically... its structure is the nucleus of modern broad-spectrum antibiotic activity

racyn

Brand of tetracycline hydrochloride

BASIC clinically...

it has a wide range of antimicrobial action in vitro and in vivo

it is well tolerated

it is effective against both gram-positive and gram-negative bacteria

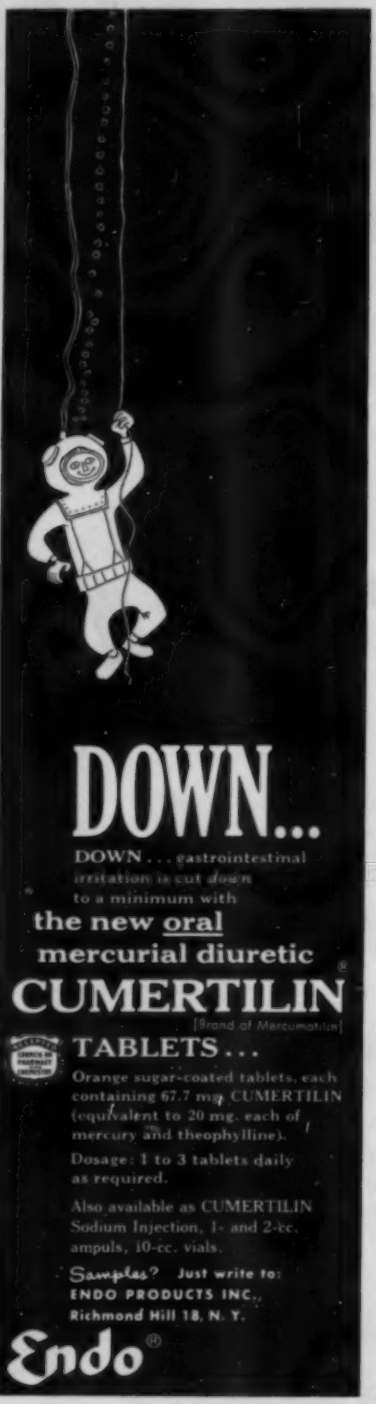
it is often effective against organisms resistant to other antibiotics, such as penicillin

it usually may be used in the presence of penicillin sensitivity or intolerance to other broad-spectrum antibiotics

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TETRACYN INTRAVENOUS Vials of 250 mg., and 500 mg.
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Vol.	XXXVIII, No.	4—April, 1953
Vol.	XXXIX, No.	1—July, 1953
Vol.	XXXIX, No.	2—August, 1953
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REFERENCE: 1. New York State J Med. 50:2293, 1950.

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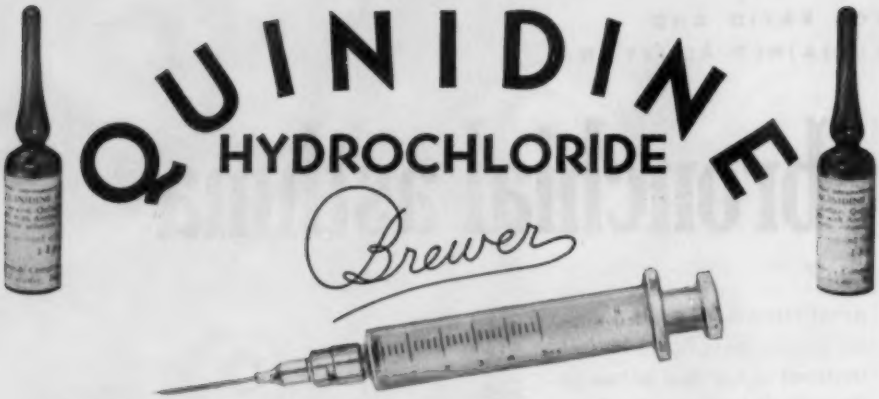
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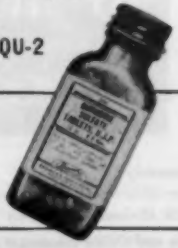
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SCHEDULE OF POSTGRADUATE COURSES, SPRING, 1954

	March		April					May		June	
(All registrations must be made through the American College of Physicians, 4200 Pine Street, Philadelphia 4, Pa. Fees: A.C.P. Members, $30.00; non-members, $60.00. Registration forms furnished on request. Detailed bulletins available from January 20, 1954.)	15–19	22–26	1–4	5–9	12–17	19–24	26–30	10–14	17–21	14–18	21–25
Course No. 1, **CLINICAL GASTRO-ENTEROLOGY:** Louisiana State University School of Medicine, New Orleans, La.; Gordon McHardy, M.D., F.A.C.P., Director	X		American Heart Assn. Meeting, Chicago	Annual Session: American College of Physicians, Chicago	Easter Week—Easter, April 18						Annual Meeting, American Medical Assn., San Francisco
Course No. 2, **SELECTED SUBJECTS IN INTERNAL MEDICINE:** Columbia-Presbyterian Medical Center, New York, N. Y.; Franklin M. Hanger, M.D., F.A.C.P., and Robert F. Loeb, M.D., F.A.C.P., Co-Directors		X									
Course No. 3, **CLINICAL ELECTROCARDIOGRAPHY:** Wayne University College of Medicine, Detroit, Mich.; Gordon B. Myers, M.D., F.A.C.P., Director						X					
Course No. 4, **CLINICAL HEMATOLOGY:** Northwestern University Medical School, Chicago, Ill.; Howard L. Alt, M.D., F.A.C.P., Director; Leon O. Jacobson, M.D., F.A.C.P., and Louis R. Limarzi, M.D., F.A.C.P., Co-Directors							X				
Course No. 5, **INTERNAL MEDICINE:** University of Pennsylvania School of Medicine, Philadelphia, Pa.; Francis C. Wood, M.D., F.A.C.P., and Calvin F. Kay, M.D., F.A.C.P., Co-Directors								X			
Course No. 6, **DISEASES DUE TO ALLERGIC AND IMMUNE MECHANISMS:** University of Pittsburgh School of Medicine, Pittsburgh, Pa.; Leo H. Criep, M.D., F.A.C.P., Director									X		
Course No. 7, **INTERNAL MEDICINE:** University of California Medical School, San Francisco, Calif.; Stacy R. Mettier, M.D., F.A.C.P., Director										X	
Course No. 8, **ISOTOPES IN CLINICAL MEDICINE:** Ohio State University College of Medicine, Columbus, Ohio; Charles A. Doan, M.D., F.A.C.P., William G. Myers, M.D., F.A.C.P., and Bruce K. Wiseman, M.D., F.A.C.P., Co-Directors										X	

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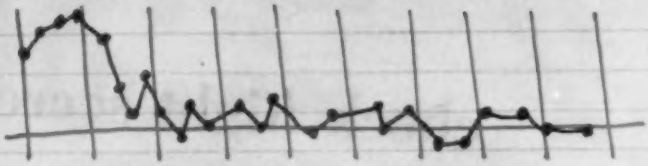
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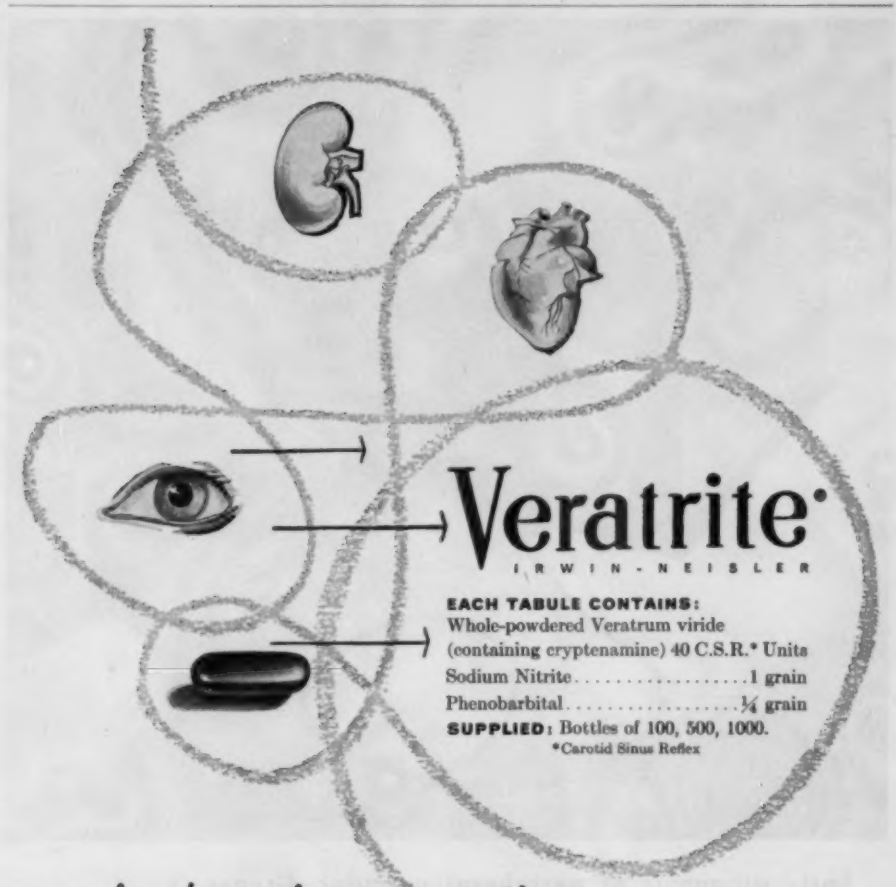
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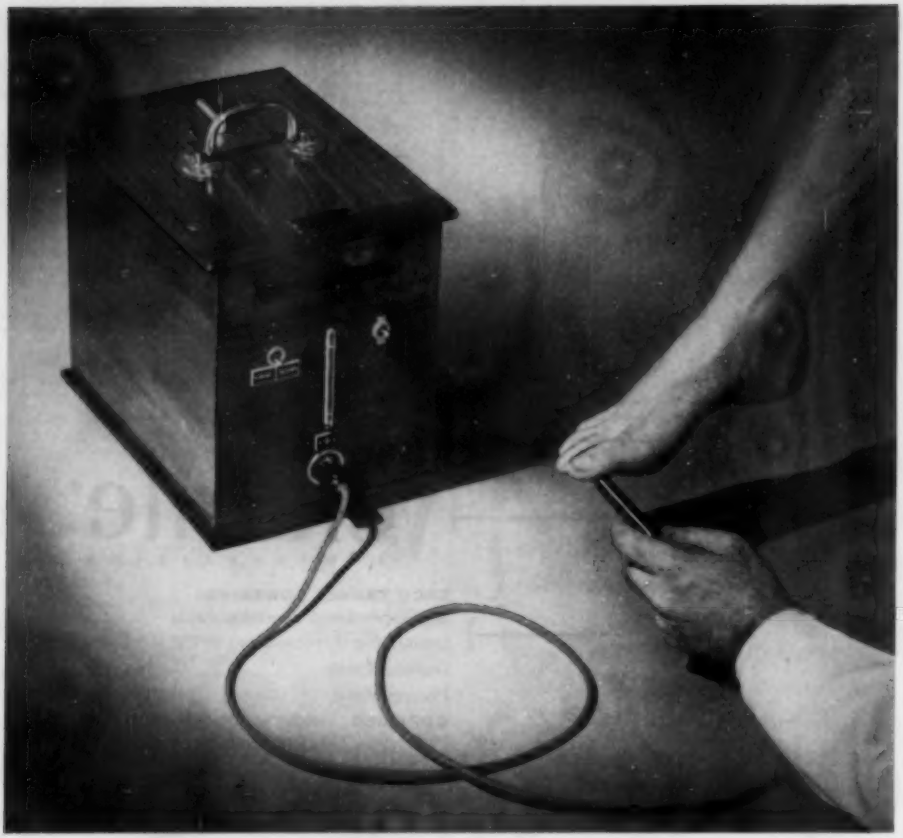
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